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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

(Mark One)

☒

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2019

Or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to .

Commission file number: 001-37539

Global Blood Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**27-4825712**
(State of other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
171 Oyster Point Boulevard, Suite 300 South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 741-7700

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	**GBT**	**The NASDAQ Global Select Market**

Securities registered under Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act.) Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant was approximately $3,070,754,389 as of June 30, 2019 based upon the closing sale price on the NASDAQ Global Select Market reported for such date. Shares of common stock held by each executive officer and director have been excluded in that such persons may be deemed to be affiliates of the registrant. Shares of common stock held by other persons, including certain holders of more than 10% of the outstanding shares of common stock, have not been excluded in that such persons are not deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 21, 2020, the registrant had 60,829,023 shares of common stock, par value $0.001, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the registrant's 2020 Annual Meeting of Stockholders, to be filed subsequent to the date hereof with the Securities and Exchange Commission, or SEC, are incorporated by reference into Part III of this report. Such proxy statement will be filed with the SEC not later than 120 days after the end of the registrant's fiscal year ended December 31, 2019.

GLOBAL BLOOD THERAPEUTICS, INC.
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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements made in this Annual Report on Form 10-K that are not statements of historical information are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements include, but are not limited to, statements regarding:

- our ability to successfully commercialize our approved product, Oxbryta® (voxelotor) tablets as well as inclacumab or any other product candidate we may identify and pursue, if approved;
- the potential market opportunity for, and rate and degree of market acceptance of, Oxbryta, inclacumab or any other product candidate we may identify and pursue, if approved;
- the benefits of the use of Oxbryta, inclacumab or any other product candidate we may identify and develop;
- the limitations of current treatment options for sickle cell disease, or SCD;
- our ability to successfully maintain a sales force and commercial infrastructure and to commercialize Oxbryta and any other approved products (if any) effectively and in compliance with complex compliance and other requirements;
- our ability to compete with companies currently commercializing or engaged in the clinical development of treatments for the disease indications that we pursue;
- our ability to manufacture Oxbryta for commercial sale and clinical development in conformity with the FDA and other applicable requirements;
- our reliance on third-party contract manufacturers to manufacture and supply Oxbryta and our product candidates;
- our expectations regarding government and third-party payor coverage and reimbursement;
- the timing and results of our continued development of Oxbryta, including, but not limited to, ongoing or planned clinical studies to satisfy post-approval confirmatory study requirements or to seek to expand approved product labeling;
- the timing and results of our preclinical studies and clinical trials of inclacumab and any other product candidate we may develop;
- our ability to leverage the safety data from prior clinical studies of inclacumab, which were not in patients with SCD, in our development of inclacumab;
- our ability to enroll patients in and complete our clinical trials at the pace we project;
- whether the results of our preclinical studies and clinical trials will be sufficient to support any or full domestic or foreign regulatory approvals for Oxbryta, inclacumab or any other product candidate we may develop;
- our ability to obtain, including under any expedited development or review programs, and maintain any or full regulatory approval of Oxbryta, inclacumab or any other product candidates we may develop;
- our ability to advance any other programs through preclinical and clinical development, and the timing and scope of these development activities;
- our ability to maintain, or to recognize the anticipated benefits of, orphan drug designation for Oxbryta or to obtain orphan drug designation for any product candidate we may identify and pursue in the United States, Europe or any other jurisdiction;
- our ability to maintain, or to recognize the anticipated benefits of, access to accelerated development and review programs through the FDA, such as the fast track and breakthrough therapy programs, or through the EMA's PRIME program, for Oxbryta or any product candidate we may identify and pursue;

- our reliance on third parties to conduct our clinical trials;
- our ability to retain and recruit key personnel;
- our ability to obtain and maintain intellectual property protection for Oxbryta or any product candidate we may identify and pursue;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements, sufficiency of capital resources and our needs for or ability to obtain additional financing;
- our financial performance;
- developments and projections relating to our competitors or our industry;
- our plans to explore strategic transactions to broaden our pipeline; and
- our ability to implement our strategic plans for our business and technology.

We have made these statements in reliance on the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are subject to certain risks and uncertainties, which could cause actual results to differ materially from those projected or anticipated. Although we believe our assumptions underlying our forward-looking statements are reasonable as of the date of this report, we cannot assure you that the forward-looking statements set out in this report will prove to be accurate. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words or other comparable terminology. Some of the factors that could cause our actual results to differ materially from our expectations or beliefs are disclosed under the caption “Risk Factors,” as well as other sections of this report that include, without limitation: the results of our commercialization of Oxbryta, the potential safety, efficacy or other therapeutic benefits of Oxbryta and our product candidates, our capital resources, commercial market estimates, the timing for initiation of, availability of data from, and completion of, our ongoing and planned clinical trials and the results of these clinical trials, the pathways for regulatory approval of Oxbryta and our product candidates, our ongoing and future research and development efforts, patent protection, effects of healthcare reform, reliance on third parties, and other risks set forth below. All forward-looking statements speak only as of the date on which they are made and we disclaim any intent to update forward-looking statements to reflect subsequent developments or actual results. Except as required by law, we assume no obligation to update any forward-looking statements publicly, or to revise any forward-looking statement to reflect events or developments occurring after the date of this report, even if new information becomes available in the future. Thus, you should not assume that our silence over time means that actual events are bearing out as previously expressed or implied in any such forward-looking statement.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

In this Annual Report on Form 10-K, unless the context requires otherwise, “GBT,” “Company,” “we,” “our,” and “us” means Global Blood Therapeutics, Inc., together with our consolidated subsidiaries. Oxbryta, GBT Source Solutions and GBT Source are trademarks of GBT. This Form 10-K also contains trademarks of third parties, and any such trademark is the property of its owner.

PART I

Item 1. *Business*

Overview

We are a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. Founded in 2011, GBT is delivering on its goal to transform the treatment and care of sickle cell disease, or SCD, a lifelong, devastating inherited blood disorder that is marked by red blood cell, or RBC, destruction and occluded blood flow and hypoxia, leading to anemia, stroke, multi-organ failure, severe pain crises, and shortened patient life span. As a result of the historic lack of treatment options, patients with SCD suffer serious morbidity and premature mortality.

It is estimated the prevalence of SCD is approximately 100,000 individuals in the United States, where newborn screening is mandatory, and approximately 60,000 individuals in Europe. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually, and SCD is concentrated in populations of African, Middle Eastern and South Asian descent.

In late November 2019, we received U.S. Food and Drug Administration, or FDA, accelerated approval for our first medicine, Oxbryta® (voxelotor) tablets for the treatment of SCD in adults and children 12 years of age and older. Oxbryta, an oral therapy taken once daily, is the first FDA-approved treatment that directly inhibits sickle hemoglobin polymerization, the root cause of SCD.

The accelerated approval of Oxbryta is based on clinically meaningful and statistically significant improvements in hemoglobin levels, accompanied by reductions in RBC destruction (hemolysis). Data from our Phase 3 HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS PolymErization) Study of 274 patients 12 years of age and older with SCD showed that, after 24 weeks of treatment, 51.1% of patients receiving Oxbryta achieved a greater than 1 g/dL increase in hemoglobin compared with 6.5% receiving placebo ($p<0.001$). The HOPE data also demonstrated corresponding improvements in other markers of hemolysis as well as a favorable safety and tolerability profile for Oxbryta.

In early December 2019, we began to make Oxbryta available to patients through our specialty pharmacy partner network. As part of this product launch, we are focused on securing reimbursement and expanding patient access. As part of our commitment to ensuring patient access, we established GBT Source Solutions™, a comprehensive program for patients who are prescribed Oxbryta that provides a wide range of practical, educational and financial support customized to each patient's needs.

We are conducting and plan to conduct additional studies of Oxbryta, including our ongoing Phase 2a HOPE-KIDS 1 Study, an open-label, single- and multiple-dose Phase 2a study that is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD, and, as a condition of accelerated approval, our Phase 3 HOPE-KIDS 2 Study, a post-approval confirmatory study we initiated in December 2019 that is using transcranial Doppler, or TCD, flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. We also expect to conduct additional clinical studies of Oxbryta, including to seek to expand the potential approved product label into younger pediatric populations.

Beyond Oxbryta, we are also engaged in other research and development activities, all of which are currently in earlier development stages. For example, we are advancing our SCD pipeline with inclacumab, a p-selectin inhibitor in development to address pain crises associated with the disease. In addition, our drug discovery team is working on new targets to develop the next generation of treatments for SCD.

As part of those efforts, we regularly evaluate opportunities to in-license, acquire or invest in new business, technology or assets or engage in related discussions with other business entities. In December 2019, we entered

into the License and Collaboration Agreement, or Syros Agreement, with Syros Pharmaceuticals, Inc., or Syros, to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the Syros Agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States. We will continue to seek the best scientific approaches to transform the treatment of these devastating lifelong diseases.

Strategy

Our mission is to discover, develop and deliver life-changing treatments for people living with grievous blood-based disorders, starting with SCD. We believe that with our first approved medicine, Oxbryta, along with the innovative patient program we have developed to accompany it, GBT Source Solutions, we are well-positioned to address many of the needs of the SCD community. Oxbryta is the first and only FDA-approved sickle hemoglobin polymerization inhibitor, a new class of therapy, and it is broadly indicated in the United States for the treatment of SCD in adults and children 12 years of age and older.

Key elements of our strategy are to:

Drive successful U.S. launch of Oxbryta. We launched Oxbryta in the United States in December 2019. Prior to this launch, our team began meeting healthcare providers, or HCPs, and payers in key markets to educate them on the role of anemia and hemolysis in SCD. Our field team, including a total of approximately 75 Sickle Cell Therapeutic Specialists and Regional Business Directors, are now focused on engaging with nearly 6,000 targeted HCPs to educate them on Oxbryta's FDA approval and broad label. In addition, our payer team is engaging government and commercial payers to secure formulary coverage of Oxbryta, with an initial focus on the 17 states where 85% of SCD patients reside, and our goal is to secure broad coverage for Oxbryta by payers by the end of 2020.

To support the launch of Oxbryta, we created GBT Source Solutions, a high-touch program for patients, their families and HCPs that is utilized when Oxbryta is prescribed. GBT Source Solutions provides a wide range of real-time, ongoing, practical, educational, and financial support customized to each patient's needs. GBT Source Solutions provides support by reviewing insurance coverage options and explaining benefits; working with the specialty pharmacy partner network to coordinate delivery of Oxbryta to wherever the patient chooses; helping with financial and co-pay assistance for eligible patients; and helping patients stay on treatment as prescribed by their treating physicians with a nurse support team. GBT Source Solutions is supported by a team of highly trained professionals and regional, field-based patient navigators that will help patients and provide resources to help HCPs understand insurance requirements and other administrative details when prescribing Oxbryta.

Expand clinical data and potential approved product labeling supporting Oxbryta. We have a comprehensive plan to continue to build clinical evidence supporting the safety and efficacy of Oxbryta, now that our Phase 3 HOPE Study that provided the support for accelerated approval of the product has concluded. This plan includes studies designed to demonstrate that improving hemoglobin and reducing hemolysis leads to an improvement in organ dysfunction—specifically focused on outcomes in the brain, lungs, kidneys and heart—and exercise capacity. We are continuing to study Oxbryta in the ongoing Phase 2a HOPE-KIDS 1 Study, an open-label, single- and multiple-dose Phase 2a study that is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD, and our HOPE-KIDS 2 Study, a Phase 3 clinical trial that we intend to satisfy the FDA's requirement for us to complete at least one post-approval confirmatory study. Initiated in December 2019, our HOPE-KIDS 2 Study is using TCD flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. In addition, we are planning a comprehensive program to gather and evaluate real world evidence and historical data to determine the long-term connection between improvements in hemoglobin and organ damage and longer-term outcomes,

with an initial focus on stroke and silent infarct. These and other aspects of our overall clinical development program for Oxbryta are also intended to position us to be able to seek approval over time for product labeling for Oxbryta for patients younger than the current age limit (12 years old), down to as young as 9 months of age.

Secure regulatory approval and launch in Europe. In Europe, there are approximately 60,000 SCD patients, the majority of which are in two countries, France and the United Kingdom. The European Medicines Agency, or EMA, has included Oxbryta in its Priority Medicines (PRIME) program, and the European Commission, or EC, has designated Oxbryta as an orphan medicinal product for the treatment of patients with SCD. We plan to meet with the EMA in the first half of 2020 to discuss the regulatory pathway for Oxbryta in Europe.

Advance inclacumab and develop next-generation of treatments for SCD and grievous blood disorders. Our strategy includes the expansion of our product pipeline through the discovery and development of novel therapeutic approaches for SCD and grievous blood disorders. Our lead product candidate is inclacumab, a novel fully human monoclonal antibody against p-selectin, a clinically validated target for the reduction of vaso-occlusive crises, or VOCs. We are developing inclacumab as a treatment for VOC in patients with SCD and expect to initiate a pivotal clinical study in 2021. We also have a collaboration with Syros to discover, develop and commercialize novel therapies for SCD and beta thalassemia utilizing Syros' gene control platform to identify therapeutic targets and discover small molecule drugs that induce fetal hemoglobin. In addition, our drug discovery and business development teams are actively working on new opportunities to expand our product pipeline.

Improve care for SCD patients worldwide. The majority of the global SCD patient population is outside of the U.S., including more than 75% of the global incidence in sub-Saharan Africa and large populations in India, the Middle East, and South America. Each of these regions represent unique challenges to providing access due to complex healthcare systems and will require a customizable approach that meets the needs of the local community. Our clinical programs include sites outside of the U.S. and all participants in our clinical trials will continue to receive Oxbryta until it is available in their countries. We are developing strategies to make Oxbryta available to all patients in these regions in a manner that is sustainable for us over the long-term.

Key 2019 Highlights

Regulatory/Commercial

- In June 2019, we announced final agreement with the FDA on the design of the post-approval confirmatory study of Oxbryta, HOPE-KIDS 2, utilizing TCD flow velocity as the primary endpoint.
- In the third quarter of 2019, we hired approximately 65 Sickle Cell Therapeutic Specialists, bringing our field team to approximately 75 members.
- In September 2019, we announced that the FDA accepted for filing our New Drug Application, or NDA, seeking accelerated approval for Oxbryta and that the FDA granted Priority Review for the NDA, which provides for a six-month review. Accordingly, our New Drug Application, or NDA, was assigned a Prescription Drug User Fee Act, as amended, or PDUFA, target action date of February 26, 2020.
- In late November 2019, three months ahead of the FDA's PDUFA target action date, the FDA granted accelerated approval for Oxbryta for the treatment of SCD in adults and children 12 years of age and older.
- Upon the approval of Oxbryta, we launched GBT Source Solutions, a comprehensive program for patients who are prescribed Oxbryta that provides a wide range of practical, educational and financial support customized to each patient's needs.
- In early December 2019, Oxbryta was first made available in the United States through our specialty pharmacy partner network.

SCD Community

- In September 2019, we hosted two SCD-focused conferences in Washington, D.C., including the 8th Annual SCD Therapeutics Conference, which highlighted the latest medical advances and future trends in the treatment of patients with SCD, and the 2019 SCD Access to Care Summit, which brought together members of the SCD community to discuss solutions toward improving access to care.
- In June 2019, we awarded more than $200,000 in grants to five non-profit organizations through our new Access to Excellent Care for Sickle Cell Patients Pilot Program (ACCEL). The program provides grant funding to support novel projects aimed at improving access to high-quality healthcare for individuals with SCD in the United States.
- In July 2019, we launched two national SCD awareness campaigns, *Sickle Cell Speaks*, a patient-focused campaign that aims to break down stigmas and misconceptions associated with the disease, and *SCD Silent Damage*, which seeks to help healthcare professionals increase their understanding of SCD and the resulting cascade of clinical complications leading to high levels of morbidity and mortality in patients.

Medical Meeting Presentations and Publications

- In June 2019, 24-week data from all participants enrolled in the Phase 3 HOPE Study were presented during the Presidential Symposium at the 2019 European Hematology Association (EHA) Annual Congress and simultaneously published in *The New England Journal of Medicine*. The study findings showed that Oxbryta provided a rapid, statistically significant and sustained improvement in hemoglobin levels and reduced the incidence of worsening anemia and hemolysis.
- Additional post-hoc analyses of the Phase 3 HOPE Study were presented at the 13th Annual Academy for Sickle Cell and Thalassemia Conference in London in October 2019 and at the 61st American Society of Hematology (ASH) Annual Meeting & Exposition in December 2019, providing greater insight into the safety and efficacy of Oxbryta.
- We presented a number of abstracts related to our SCD research programs, including a study quantifying the impact of raising hemoglobin on TCD flow velocity levels in a real-world setting that provided increased confidence in the probability of success of our now ongoing post-approval confirmatory study of Oxbryta. The study examined children treated with hydroxyurea, and, over an observation period of up to four years, results showed that a therapeutic rise in hemoglobin was significantly associated with a reduction in TCD levels.
- In January 2019, results from our Phase 1/2 study and the open-label extension demonstrating the safety, tolerability, pharmacokinetic and pharmacodynamic properties of Oxbryta in patients with SCD were published in Blood.

Corporate

- In June 2019, we raised approximately $198.1 million in net proceeds from an underwritten public offering and in December 2019, we entered into a $150.0 million loan agreement with funds managed by Pharmakon Advisors LP, a leading global life sciences investment firm, and drew down the first tranche of $75.0 million with the close of the transaction.
- In December 2019, we entered into a collaboration with Syros to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States.

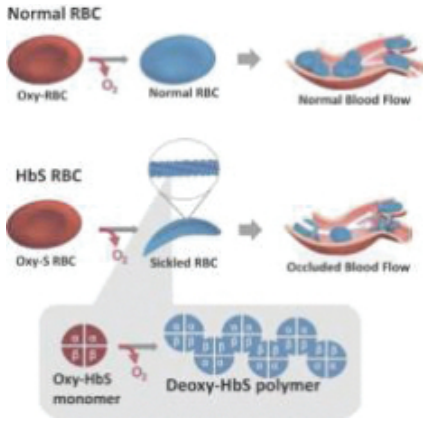
- We appointed a chief scientific officer and a chief human resources officer to our senior management team.

Overview of SCD

SCD is a devastating and rare inherited blood disorder that impacts hemoglobin, a protein carried by RBCs that delivers oxygen to tissues and organs throughout the body. It attacks every organ in the body and causes a wide range of complications, including inflammation, multi-organ damage and failure and early death. Many of these start with anemia and hemolysis. Beginning in childhood, patients suffer unpredictable and recurrent episodes or crises of severe pain due to blocked blood flow to organs, which often lead to physical and psychosocial disability. In addition, the constant destruction of RBCs with the release of their contents into the blood often leads to damaged or diseased blood vessels, which further exacerbate blood flow obstruction and multi-organ damage. Consequences of SCD can manifest in early childhood and may include stroke, spleen failure, pulmonary hypertension, acute chest syndrome, liver disease, kidney failure, leg ulcers, priapism, which is a medical emergency due to refractory penile erection, and premature death. In the United States, SCD has been estimated to shorten patient life expectancy by approximately 30 years even with available medical care.

SCD is a genetic blood disorder caused by a single gene mutation in the beta-chain of hemoglobin, which results in mutant hemoglobin known as HbS. Hemoglobin is the protein in RBCs that carries oxygen from the lungs to the body's tissues, releases oxygen at the tissues, and returns carbon dioxide from the tissues back to the lungs. Hemoglobin accomplishes this by binding and then releasing oxygen through allosterism, which means the hemoglobin molecule changes its shape to have a high affinity for oxygen in the lungs, where oxygen is abundant, and to have a low affinity for oxygen in the tissues, where oxygen must be released. Oxyhemoglobin, the high oxygen affinity form of hemoglobin, is formed in the lungs during respiration, when oxygen binds to the hemoglobin molecule. Deoxyhemoglobin, the low oxygen affinity form of hemoglobin, is formed when oxygen molecules are removed from the binding site as blood flows from the lungs to the tissues in the body. In patients with SCD, deoxygenated HbS, molecules polymerize to form long, rigid rods within an RBC, much like a "sword within a balloon." As a consequence, the normally round and flexible RBC becomes rigid and elongate into a "sickled" shape. Sickled RBCs do not flow properly in the bloodstream; they clog small blood vessels and reduce blood flow to the organs. This results in inadequate oxygen delivery, or hypoxia, to all body tissues, which can lead to multi-organ failure and premature death.

The following graphic illustrates the process by which sickling occurs in SCD patients as a result of the polymerization of deoxygenated HbS in an RBC, leading to occluded blood flow, in contrast to a normal RBC:



SCD manifests in individuals who inherit at least one HbS gene from a parent and an additional mutation on the second beta globin gene from the other parent. There are several different genotypes of SCD, including the following major genotypes:

- HbSS, or sickle cell anemia, where both genes are HbS;
- HbSC, where one gene is HbS, and the other is HbC (inherited by a non-SCD impacted parent); and
- HbS/ßthal, where one gene is HbS, and the other is Beta thalassemia.

SCD Patient and Community Impact

The Centers for Disease Control and Prevention, or CDC, estimates the prevalence of SCD at approximately 100,000 individuals in the United States, where newborn screening is mandatory. The incidence of SCD is estimated at approximately 1 in 2,000 to 2,500 newborns in the United States. It is estimated that the prevalence of SCD in Europe is approximately 60,000 individuals. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually. SCD is concentrated in populations of African, Middle Eastern and South Asian descent.

Of SCD patients in the United States, approximately 45% are under the age of 18, and approximately 60% to 65% have the HbSS genotype, which is often referred to as sickle cell anemia, with the remaining 35% to 40% having other genotypes. In all genotypes of SCD, the mechanism that leads to the consequences of the disease involves the polymerization of HbS in its deoxygenated state, which results in RBC sickling. We believe that because of this common underlying mechanism, Oxbryta may show activity across all SCD genotypes. Our Phase 3 HOPE Study enrolled SCD patients with all genotypes of SCD.

SCD is associated with a high healthcare utilization and economic burden. It is estimated that in the United States, the annual cost of medical care for an SCD patient with complications is up to $286,000 and that end-organ damage drives major healthcare utilization, with an average SCD patient receiving healthcare services for 30 to 54 days per year. In addition, there is potential for a significant financial burden on patients and society: it is estimated that SCD patients are deprived of approximately $700,000 in lost lifetime income, not including the impact on caregiver productivity. As a result, we believe that a safe, effective and convenient oral treatment for SCD has the potential to be well received by patients, physicians and payors.

Other Current Treatment Options

SCD remains a significant unmet medical need. Despite a dramatic increase in orphan drug approvals by the FDA in recent years, for many years there had been limited innovation in SCD.

The first drug approved to treat SCD, known as hydroxyurea, which was initially approved as a chemotherapy drug, was approved by the FDA in 1998 for the treatment of sickle cell anemia in adults with three or more painful crises per year. Hydroxyurea is not approved for pediatric SCD patients in the United States. The use of hydroxyurea is significantly limited by its side effect profile, variable patient responses and concerns regarding long-term toxicity. Hydroxyurea’s side effects include impairment of fertility, suppression of white blood cells, or neutropenia, and suppression of platelets, or thrombocytopenia, which place patients at risk for infection and bleeding.

In July 2017, the FDA approved L-glutamine oral powder for patients age five and older with SCD to reduce severe complications associated with the disorder. In January 2018, Emmaus Life Sciences, Inc., the marketer for Endari® (L-glutamine oral powder) announced the availability of the product to patients. Endari is supplied to patients as powder that requires a large volume administration (5 grams—15 grams) mixed with liquid or food twice a day. In November 2019, the FDA approved Adakveo® (crizanlizumab) to reduce the frequency of VOCs, or pain crises, in adult and pediatric patients aged 16 years and older with SCD, and it was made available to patients before the end of 2019. Crizanlizumab is administered via a 30-minute intravenous, or IV, infusion given once per month by a health care provider.

In addition to treatment with hydroxyurea, L-glutamine and crizanlizumab, transfusions with normal blood are an option to help alleviate anemia, which is a common symptom of SCD, and reduce sickling of RBCs. Blood transfusions have a number of limitations, including the expense of treatment, lack of uniform accessibility and risks ranging from allergic reactions to serious complications such as blood-borne infection and iron overload, which can cause organ damage. The only potentially curative treatment currently available for SCD patients is bone marrow transplantation, which requires a suitable matching donor and carries significant risks, including an approximately 5% mortality rate. Despite these other current treatment options, blood transfusion and palliative therapy for acute pain attacks, patients with SCD continue to suffer serious morbidity and premature mortality.

In light of the devastating effects of SCD on patients and the high costs of care for these patients, there has been a significant unmet need for a treatment that:

- inhibits abnormal hemoglobin polymer formation, the underlying mechanism of RBC sickling;
- stops inappropriate RBC destruction and improves blood flow and oxygen delivery to tissues;
- reduces hemolytic anemia that leads to chronic organ damage and early mortality in patients with SCD;
- prevents or reduces the episodes or crises of severe pain associated with SCD;
- modifies the long-term course of the disease;
- is effective in all SCD genotypes and in both children and adults;
- has a more favorable side effect profile than currently available therapies; and
- is available as a convenient, oral therapy.

Oxbryta—Our Newly Marketed Medicine

In November 2019, we received FDA accelerated approval for Oxbryta for the treatment of SCD in adults and children 12 years of age and older. Oxbryta, an oral, once-daily therapy, is the first FDA-approved treatment that directly inhibits sickle hemoglobin polymerization, the root cause of SCD. We believe the label for Oxbryta highlights several important attributes for physicians and patients, including:

- A broad indication for use with no hemoglobin level restrictions and no clinically significant differences in the pharmacokinetics based on age, sex, body weight or mild to severe renal impairment
- A specific description of Oxbryta as a hemoglobin S polymerization inhibitor that may inhibit RBC sickling, improve RBC deformability, and reduce whole blood viscosity
- No restriction on use with or without hydroxyurea
- Clinical data highlights from the HOPE Study, including the subject-level change from baseline in hemoglobin at week 24 in patients who completed 24 weeks of treatment with Oxbryta 1500 mg dose or placebo

Overview of Hemoglobin Biology and Oxbryta's Mechanism of Action

Hemoglobin transports oxygen from the lungs to the body's tissues, releases oxygen into the tissues, and returns carbon dioxide from the tissues back to the lungs by changing its shape to be high affinity for oxygen in the lungs, where oxygen is abundant, and low affinity for oxygen in the tissues, where oxygen must be released. An important tool for assessing how readily hemoglobin acquires and binds oxygen in the lungs and releases oxygen into the tissues is the oxygen equilibrium curve, or OEC. The OEC represents the proportion of oxyhemoglobin, measured as the percentage of oxygen saturation (O2 % saturation) on the vertical axis relative to the amount of oxygen dissolved in blood, indicated as the oxygen tension, or partial pressure of oxygen (pO2) measured in millimeters of mercury (mmHg), on the horizontal axis.

We have demonstrated in preclinical models that our novel hemoglobin modifiers, including Oxbryta, bind to hemoglobin, resulting in increased oxygen affinity. The effect of Oxbryta on the measured OEC is a shift of the curve to the left. In other words, at a given prevailing oxygen tension in the blood, we have observed a higher percentage of oxygen saturation, or a higher proportion of oxyhemoglobin in the blood, following the administration of Oxbryta.

In several studies of SCD, scientists have demonstrated that hemoglobin in the oxygenated state is a potent inhibitor of HbS polymerization. Since HbS polymerization occurs in the deoxygenated state, we believe that increasing the proportion of oxyhemoglobin, or "left-shifting" the OEC, should delay the polymerization of HbS and prevent the sickling of RBCs, which may ameliorate many of the clinical manifestations of SCD. Importantly, we are able to measure the proportion of hemoglobin modification (%HbMOD), which is expressed as the percentage of hemoglobin molecules occupied or bound by Oxbryta.

HbF, which is present during fetal development and persists for up to six to nine months in infants until it is replaced by adult hemoglobin, has an inherent high affinity for oxygen, which is critical for a developing fetus to capture oxygen from the mother's blood. Newborns with SCD do not experience RBC sickling until approximately six to nine months of age, after which HbF is no longer expressed. Additionally, it has been observed that rare individuals who have inherited the HbS mutation and a gene deletion that allows them to continue to express 10% to 30% HbF in their RBCs into adulthood do not exhibit the clinical manifestations of SCD, despite expressing up to 90% HbS in their blood. HbF dilutes the concentration of deoxygenated HbS that can participate in polymerization, and, thereby, prevents hemoglobin polymer from forming.

Based on these observations, we believe that to delay polymerization of HbS, Oxbryta would need to bind to only approximately 10% to 30% of the total hemoglobin in a patient's blood. One theoretical concern regarding increasing the affinity of hemoglobin for oxygen is that excessive oxygen affinity could prevent hemoglobin from releasing oxygen into the tissues, thus causing hypoxia. However, we have not observed any findings from our clinical programs that demonstrated any evidence of such tissue impairment. Based on HbF data, our animal toxicology studies, and our clinical studies, we believe our target modification of the total hemoglobin in a patient's blood would not adversely compromise oxygen delivery to the tissues. This is supported by exercise testing we have performed in SCD patients and healthy volunteers showing normal oxygen consumption and the absence of a dose level or exposure related increase in erythropoietin levels in patients enrolled in the HOPE Study.

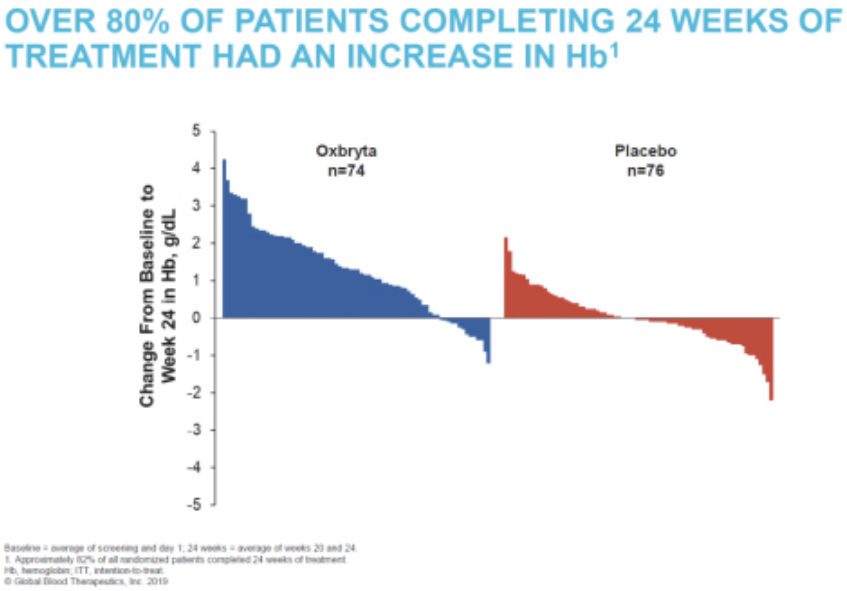
Oxbryta increases hemoglobin's affinity for oxygen by binding to the alpha-chain of hemoglobin. Oxbryta has been observed to keep a proportion of HbS in its oxygenated state so it cannot participate in polymerization. Similar to HbF, by diluting total HbS with a proportion of Oxbryta-bound hemoglobin, Oxbryta prevents hemoglobin polymer formation. Based on its mechanism of action, we believe that Oxbryta can reduce the physical and clinical manifestations of SCD.

Overview of Phase 3 and Ongoing Oxbryta Clinical Trials

Phase 3 HOPE Study

We recently completed a randomized, double-blind, placebo-controlled, multi-national Phase 3 clinical trial of Oxbryta in adult and adolescent patients with SCD that we refer to as the HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS PolymErization) Study, the interim results of which we used as the basis for our accelerated approval under Subpart H of FDA's NDA regulations. Data from the Phase 3 HOPE Study of 274 patients 12 years of age and older with SCD showed that the HOPE Study met its primary endpoint of an improvement in hemoglobin greater than 1 g/dL at 24 weeks with Oxbryta 1500 mg compared with placebo: After 24 weeks of treatment, 51.1% of patients receiving Oxbryta achieved a greater than 1 g/dL increase in hemoglobin compared with 6.5% receiving placebo ($p<0.001$). In addition, the data demonstrated corresponding improvements in other markers of hemolysis as well as a favorable safety and tolerability profile for Oxbryta. These interim Phase 3 HOPE data were published in the June 2019 issue of the *New England Journal of Medicine*.

In connection with the accelerated approval of Oxbryta, we have agreed with the FDA to submit the final study report by September 2020. We also agreed with the FDA to complete at least five years of follow-up for all patients on treatment and submit to the FDA interim reports each year in June from 2021 to 2025.



Additional Studies

We are conducting and plan to conduct additional clinical trials of Oxbryta, including our ongoing Phase 2a HOPE-KIDS 1 Study, our recently initiated Phase 3 HOPE-KIDS 2 Study and our recently initiated dose optimization study.

Phase 2a HOPE-KIDS 1 Study

We are continuing to evaluate the safety and pharmacokinetics of single and multiple doses of Oxbryta in adolescent and pediatric patients with SCD in an ongoing Phase 2a clinical trial, which we call the HOPE-KIDS 1 Study. Initiated in August 2016, our ongoing HOPE-KIDS 1 Study is an open-label, single- and multiple-dose Phase 2a study that is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD. Part A of the study evaluated a single 600 mg dose of Oxbryta in 13 patients aged 6 to 17 years, while Part B was designed to explore Oxbryta at doses of 900 mg and 1500 mg per day administered to 40 patients ages 12 to 17 for 24 weeks. Part C of the study will evaluate Oxbryta at 1500 mg dose (or weight-based equivalent) in patients age 4 to 17 years for up to 48 weeks, and Part D of the study will evaluate the safety of Oxbryta at the weight based equivalent of 1500 mg in patients age 9 months to under 4 years as measured by Treatment Emergent Adverse Events, or TEAEs, and Serious Adverse Events, or SAEs.

Part A pharmacokinetics, or PK, data in adolescents (12 to 17 years) demonstrated that the PK and half-life of Oxbryta were similar in adolescents and adults with results supporting once-daily dosing. Part A data for pediatric patients (6 to 11 years) demonstrated that PK exposures were higher in children compared with adolescents and adults, which informed dose selection for future pediatric studies in children under 12 years of age.

The primary objective of Part B was to assess the effect of Oxbryta on anemia. Secondary objectives include effect on clinical measures of hemolysis and PK profile. Additionally, we were able to assess the exploratory

endpoint of TCD flow velocity measures in this study as TCD is a measure of stroke risk in pediatric and adolescent SCD patients. TCD measurement was not a primary or secondary endpoint or eligibility criteria in the HOPE KIDS-1 Study. Part B demonstrated a hematologic response to Oxbryta therapy, as evidenced by improvements in one or more markers of hemolysis and anemia (hemoglobin, unconjugated bilirubin and percentage reticulocyte counts).

Part C is currently enrolling patients age 4 to 17 years and will assess, as its primary endpoint, change in cerebral blood flow as measured by TCD flow velocity. Secondary measures include effect on clinical measures of hemolysis, change in cerebral blood flow and PK profile. We currently expect to complete the study in 2022.

Part D is expected to begin enrolling patients age 9 months to under 4 years in the first half of 2020, and will assess, as its primary endpoint, the safety of a weight based equivalent of 1500 mg. Secondary measures include effect on clinical measures of hemolysis and PK profile.

Phase 3 HOPE-KIDS 2 Study

As a condition of accelerated approval of Oxbryta in the United States, and to potentially obtain full regulatory approval for Oxbryta, we will continue to study Oxbryta in the HOPE-KIDS 2 Study, a post-approval confirmatory study we initiated in December 2019 that is using TCD flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. Initiated in December 2019, HOPE-KIDS 2 is a randomized, placebo-controlled Phase 3 trial that will enroll approximately 220 patients with conditional TCD flow velocity (170-199 cm/sec) at about 50 sites in the United States, Europe and Africa. The primary objective of the study is to evaluate the effect of Oxbryta on reducing the risk of stroke in children with SCD at 24 weeks months using mean change in TCD levels. Key secondary measures include conversion to normal or abnormal TCD at 96 weeks, change in hemoglobin over time and effect on clinical measures of hemolysis. The overall treatment period will be 96 weeks, and, in connection with the accelerated approval of Oxbryta, we have agreed with the FDA to submit the interim study report by July 2025, complete the trial by March 2026 and to submit the final study report by September 2026.

Dose Optimization Study

As part of our overall life cycle management for Oxbryta, we recently initiated a Phase 2 clinical trial to assess higher doses of Oxbryta, up to 3000 mg per day.

General

The HOPE-KIDS 1 Study, the HOPE-KIDS 2 Study and other aspects of our overall clinical development program for Oxbryta are also intended to position us to be able to seek approval over time for product labeling for Oxbryta for patients younger than the current age limit (12 years old), down to as young as 9 months of age.

Sales and Marketing

We assembled our commercial team and infrastructure, including approximately 75 internal sales personnel, key payer account management, marketing and patient and distribution support, ahead of our FDA approval of Oxbryta as part of our plan to commercialize Oxbryta as soon as practicable after approval. As such, we were able to make Oxbryta available in early December 2019. We expect to be able to efficiently support the commercial launch of Oxbryta with this targeted commercial organization. This expectation is due in part to the relatively limited number of SCD patients in the United States and them being primarily located in only 17 states. In addition, the prescribing audience is concentrated as many SCD patients receive care from a hematologist or another sickle cell care provider.

We are also providing a comprehensive patient support program, called GBT Source Solutions, to support our commercialization. This high-touch support program helps patients through the entire process by

(i) reviewing insurance coverage options and explaining benefits; (ii) working with the specialty pharmacy partner network to coordinate delivery of Oxbryta to wherever the patient chooses; (iii) helping with financial and copay assistance for eligible patients; and (iv) helping patients stay on treatment as prescribed by their treating physicians with a nurse support team.

With respect to commercializing Oxbryta outside of the United States, we are beginning to build a small team and additional capabilities that may be necessary to effectively support such potential commercialization, subject to any required approval. These capabilities will likely focus on a limited number of core European markets, where SCD is prevalent. Where appropriate, we may also utilize strategic partners, distributors or contract sales forces to expand the commercial availability of Oxbryta.

We currently do not expect that we will require large pharmaceutical partners for the commercialization of Oxbryta or our product candidates, although we may consider partnering in certain territories, New Molecular Entities, or NMEs, or indications for other strategic purposes. We intend to continue to evaluate our commercialization strategy as we advance our preclinical programs in other rare disease indications.

Competition

The biopharmaceutical industry is highly competitive. There are many public and private biopharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. In addition, the number of companies seeking to develop and commercialize products and therapies similar to Oxbryta and our product candidates is likely to increase.

With respect to Oxbryta, we expect to face competition from the three currently FDA-approved treatments: hydroxyurea (marketed as DROXIA or Hydrea by Bristol-Myers Squibb Company as well as in generic form), approved to reduce the frequency of painful crises and need for blood transfusions in patients with sickle cell anemia for the treatment of adults with SCD; Endari (marketed by Emmaus), approved to reduce acute complications of SCD in patients age five years and older; and crizanlizumab (marketed by Novartis), approved to reduce the frequency of VOCs in adult and pediatric patients aged 16 years and older with SCD. Several companies are also developing product candidates for chronic treatment in SCD, and several other companies are in early clinical trials to investigate new mechanisms of action for the chronic treatment of SCD. We also may face competition from one-time therapies for patients with severe SCD, including hematopoietic stem cell transplantation, gene therapy and gene editing. For example, bluebird bio, Inc., is currently engaged in the clinical development of LentiGlobin BB305, which aims to treat SCD by inserting a functional human beta-globin gene into the patient's own hematopoietic stem cells, or HSCs, ex vivo and then transplanting the modified stem cell into the patient's bloodstream. Bluebird has indicated its plans to pursue an accelerated development and approval pathway for its gene therapy product in SCD. Several agents are also in development for the treatment of VOC in patients with SCD.

Some of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

European Union Regulatory Path for Oxbryta

We have been engaged in discussions with European regulatory authorities to define the regulatory pathways for marketing authorization for Oxbryta. The objectives of these regulatory interactions include discussion of pivotal study design, trial endpoints and the continued development of Oxbryta, including in pediatric patients. We expect to provide an update on the EU regulatory pathway in the first half of 2020.

In November 2016, the European Commission, or EC, granted Orphan Drug Designation status in the European Union, or EU, for Oxbryta for the treatment of SCD. In June 2017, the EMA granted PRIME designation for Oxbryta for the treatment of SCD. The PRIME program is a regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need.

Manufacturing

We are commercializing a solid oral formulation of a tablet form of Oxbryta, and we believe we have obtained an adequate supply of Oxbryta to satisfy our immediate commercial, clinical and nonclinical demands. We are also developing a pediatric formulation of Oxbryta for use in clinical trials.

With respect to manufacturing, we do not own or operate or have any plans to establish any manufacturing facilities. We currently depend on third-party contract manufacturing organizations, or CMOs, for all of our requirements of raw materials, drug substance and drug product for our commercial, clinical and nonclinical activities for our portfolio, and we have entered into commercial manufacturing agreements with some of our CMOs to support Oxbryta commercialization. We intend to continue to rely on CMOs for the commercialization as well as continued development of Oxbryta, as well as the development and commercialization of any other product candidates, including inclacumab. Although we rely on CMOs, we have personnel and third-party consultants with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

To decrease the risk of an interruption to our drug supply, when we believe it is reasonable for us to do so, we source materials from multiple suppliers so that, in general, the loss of any one source of supply should not have a material adverse effect on commercial production, project timelines or inventory of supplies for our studies or clinical trials. However, currently we have only one or a limited number of suppliers for some of these materials for Oxbryta and for other programs, and the loss of a primary source of supply could potentially delay the availability of Oxbryta or delay our development programs. We intend to maintain a safety stock of certain materials to help avoid delays in production, but we do not know whether such stock will be sufficient. In addition, while we currently have only one commercial manufacturer for drug substance and finished drug product for Oxbryta, we have identified potential second sources and are working to establish additional sources of commercial supply. There is no guarantee as to if or when we may establish such additional sources or whether they will be adequate in all circumstances we may encounter.

Development Pipeline

Our goal is to build a robust product pipeline focused on the discovery and development of novel therapeutic approaches for SCD and grievous blood disorders. We have an active business development strategy that may provide new opportunities to expand our product pipeline with next-generation treatments for SCD. To this end, we have entered into agreements with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, “Roche”) and Syros.

License Agreement with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc.

In August 2018, we entered into the License Agreement, or Roche Agreement, with Roche pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and

know-how to develop and commercialize inclacumab, a novel fully human monoclonal antibody against p-selectin, including any modified compounds targeting p-selectin and derived from inclacumab, for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use.

We are developing inclacumab as a treatment for VOCs in patients with SCD, and we expect to be able to leverage the safety data from Roche's prior clinical studies, which were not in patients with SCD, as we proceed with our development of inclacumab. We expect to submit an Investigational New Drug application, or IND, to the FDA for inclacumab in 2021.

Under the Roche Agreement, we paid Roche an upfront payment of $2.0 million, and we will pay Roche up to an aggregate of $125.5 million in milestone payments for the SCD indication, including up to $40.5 million based on achievement of certain clinical development and regulatory milestones for inclacumab in the sickle cell disease indication, and up to $85.0 million based on achievement of certain thresholds for annual net sales of inclacumab. We will also pay Roche up to an additional $5.5 million in milestone payments, which are owed to a third party, based on achievement of such clinical development and regulatory milestones for inclacumab. We will also pay Roche up to $19.25 million in milestone payments based on achievement of certain clinical development and regulatory milestones for inclacumab for any other indication than the SCD indication. We have the right to sublicense our rights under the Roche Agreement to our affiliates without Roche's consent. Subject to certain conditions and limitations, including Roche's right of first negotiation described below, we will also have the right to sublicense our rights under the Roche Agreement to non-affiliates pursuant to partner agreements with Roche's prior written consent, which will not be unreasonably withheld or delayed. If at any time prior to the expiration of royalty or other payment obligations under the Roche Agreement, or the earlier termination of the Roche Agreement, we intend to enter into a partner agreement to sublicense rights to inclacumab, then Roche will have a right of first negotiation during an exclusivity period to negotiate in good faith with us the terms and conditions of such proposed transaction.

Collaboration with Syros Pharmaceuticals, Inc.

In December 2019, we entered into the Syros Agreement to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover small molecule drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license, with the right to sublicense, under relevant intellectual property rights and know-how of Syros arising from the collaboration, to develop, manufacture and commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States. If we exercise the option, we will be responsible for all development, manufacture, regulatory activities and commercialization of the compound or product. Syros and we will be responsible for our own costs incurred to conduct research activities, except that we will fund up to $40.0 million in preclinical research for at least three years. Unless earlier terminated or extended, the research program under the agreement will end on the third anniversary of the agreement.

Under the Syros Agreement, we paid Syros an upfront payment of $20.0 million, and, if we exercise the option, we may be obligated to pay Syros up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration. We will also be obligated to pay Syros, subject to certain reductions, tiered mid- to high-single digit royalties as percentages of calendar year net sales on any product resulting from the collaboration.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents and patent applications intended to cover Oxbryta and our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions

that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We plan to continue to expand our intellectual property portfolio. We endeavor to promptly file domestic and international patent applications for new commercially valuable inventions, including applications directed to compositions and methods of treatment created or identified from our ongoing development of our product candidates. Our success will depend in part on our ability to obtain and maintain patent and other proprietary rights protecting our commercially important technology, inventions and know-how related to our business, defend and enforce our current and future issued patents, if any, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our intellectual property portfolio.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent, if any, is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any patents, if issued, will provide sufficient protection from competitors for our business.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine the priority of inventions.

Patents

Our patent portfolio includes multiple issued U.S. patents, as well as multiple U.S. and foreign patent applications in various stages of prosecution or allowance. Our primary patents and patent applications relate to our general HbS intellectual property portfolio, which includes Oxbryta and its development program and/or analogs.

Our HbS intellectual property portfolio is comprised of multiple patent families of patents and patent applications relating to Oxbryta and/or analogs that inhibit Hb polymerization. These patent families include patents and patent applications specifically related to Oxbryta, covering certain compositions of matter, methods of use, method of manufacture, formulations, and polymorphs of Oxbryta and analogs. These patent applications are pending in a variety of jurisdictions, including the United States, jurisdictions under the Patent Cooperation Treaty and other countries.

With regard to Oxbryta specifically, we are the sole owner of issued U.S. patents covering Oxbryta, including its composition of matter, methods of use, formulations and polymorphs of Oxbryta. These issued U.S. patents covering Oxbryta will expire between 2032 and 2037, absent any applicable patent term extensions. Any patents that may issue from our pending patent applications relating to Oxbryta in the United States or from corresponding foreign patent applications, if issued, are expected to expire between 2032 and 2037, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and Regents of the University of California, or the Regents, as described below.

Our other patents in our HbS intellectual property portfolio are comprised of additional issued U.S. patents covering Oxbryta analogs. These patents, and any patents that may issue from our pending patent applications relating to Oxbryta analogs in the United States or from corresponding foreign patent applications, if issued, are

currently expected to expire between 2032 and 2039, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and the Regents, as described below.

In addition, we have exclusively licensed from the Regents worldwide patent rights covering Oxbryta and certain Oxbryta analogs, some of which patent rights we jointly own with the Regents. In exchange for our exclusive license, we have agreed to pay a royalty to the Regents of less than 1% on future net sales and to use commercially reasonable efforts to develop, manufacture, market and sell the products covered by the licensed patents. The risks associated with joint ownership of patent rights are more fully discussed under "Risk Factors—Risks Related to Our Intellectual Property."

Beyond our HbS intellectual property portfolio, we own other issued U.S. and foreign patents, seek to obtain additional issued patents, and file patent applications relating to our other research and development programs over time.

Patent term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority, assuming that all maintenance fees are paid. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO, the extent of which is offset by delays by the patent owner before the USPTO in obtaining the patent. In some cases, the term of a U.S. patent is shortened by a terminal disclaimer that reduces its term to that of an earlier-expiring patent. The term of a U.S. patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, have analogous patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. Following the FDA approval of Oxbryta, we applied for patent term extension Oxbryta, and we would expect to do the same for any other eligible product candidate that receives FDA approval in the future.

Trade secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors and contractors. These agreements generally provide that all confidential information developed or made known during the course of an individual or entities' relationship with us must be kept confidential during and after the relationship. These agreements also typically provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control,

approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products. Pricing of such products is also subject to regulation in many countries. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. drug development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States. The process generally involves the following:

- completion of extensive nonclinical studies in accordance with applicable regulations, including the FDA's GLP regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices, or GCPs, and other clinical-trial related regulations to establish the safety and efficacy of the investigational drug for each proposed indication;
- submission to the FDA of an NDA for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA whether to accept it for filing and review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with current good manufacturing practices, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the nonclinical study and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

The nonclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any of our product candidates, will be granted on a timely basis, or at all. The data required to support an NDA are generated in two distinct development stages: nonclinical and clinical. The nonclinical development stage generally involves synthesizing the active

component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing in humans. As the drug sponsor, we must submit the results of the nonclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans, and must become effective before human clinical trials may begin.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Clinical trials

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3 trials, which may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the product candidate.
- Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose of the product candidate required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve large numbers of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product candidate for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product candidate and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval, to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA. In addition, as part of an accelerated approval such as we received for Oxbryta under the FDA's Subpart H regulations, at least one post-marketing study to verify clinical benefit is required.

As the drug sponsor, we must submit progress reports detailing the results of the clinical trials and other information at least annually to the FDA, as well as written IND safety reports to the FDA and the study investigators for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing suggesting a significant risk to humans exposed to the drug and any clinically important increase in

the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must include methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

A manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product or regenerative advanced therapy.

NDA and FDA review process

The results of nonclinical studies and clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug and proposed labeling, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product's identity, strength, quality and purity. FDA approval of an NDA must be obtained before a drug may be legally marketed in the United States.

Under PDUFA, each NDA is typically accompanied by a user fee (adjusted on an annual basis). According to the FDA's fee schedule, effective through September 30, 2020, the user fee for an NDA is $2,942,965. PDUFA also imposes an annual prescription drug product program fee for human drugs ($325,424). Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business having fewer than 500 employees. Additionally, an application for a product that has been designated as a drug for a rare disease or condition (referred to as an orphan drug) under section 526 of the FDCA is not subject to an application fee unless the application includes an indication for other than a rare disease or condition. Oxbryta for the treatment of SCD has been granted orphan drug designation by the FDA and by the EC.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA is supposed to make a decision on accepting an NDA for filing within 60 days of receipt of the submission. Once the NDA is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA is supposed to complete its initial review of an NDA that it has accepted for review and respond to the applicant

within stated periods (within 10 months for a standard NDA and six months for an NDA designated by the agency for priority review). However, the FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product (including the facilities of contract manufacturers, if applicable) to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may also audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. There are likely to be extensive discussions between the FDA and the applicant during the review process. The review and evaluation of an NDA by the FDA is very comprehensive and time consuming and may take longer than originally planned to complete.

In addition, under Subpart H of the FDA's NDA regulations, which governs accelerated approval, the FDA may approve an NDA for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. The FDA grants accelerated approval under Subpart H for new drugs that address serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments, and the NDA for Oxbryta was approved by the FDA under Subpart H. Drugs approved under Subpart H, such as Oxbryta, are required to be further evaluated in at least one post-marketing study to verify clinical benefit. As a condition of accelerated approval, the FDA may also impose marketing restrictions to limit distribution or use to assure safe use of the drug, although the FDA did not impose any such requirements for the accelerated approval of Oxbryta. Pursuing accelerated approval under Subpart H does not ensure faster development timelines or ensure regulatory approval.

After the FDA evaluates an NDA, it will issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter indicates that the review cycle of the application is complete and the application will not be approved in its present form, and usually describes all of the specific deficiencies in the NDA identified by the FDA. The complete response letter may require additional clinical data and/or additional clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application, or request a hearing. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

United States Orphan drug designation

We were granted orphan drug designation by the FDA in 2015 for Oxbryta for the treatment of SCD. Under the Orphan Drug Act in the United States, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States (or more than 200,000 individuals in the United States when there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug). Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation

does not convey any advantage in or shorten the duration of the regulatory review and approval process, but does confer other potential development and commercialization benefits as described below.

Our NDA seeking approval for Oxbryta for the treatment of SCD qualified for the orphan user fee exemption from the PDUFA application fee. In addition, we should qualify for additional incentives, including tax credits for qualifying clinical trials of Oxbryta, and Oxbryta will also qualify for a substantial period of market exclusivity. If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety, or by providing a major contribution to patient care. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product for a different indication than that for which the orphan product has exclusivity. A competitor could also block the approval of one of our products for seven years by obtaining orphan product exclusivity for the same product (or a competitor product that contains our product candidate) for the same indication we are seeking. If a drug designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union, or EU, has similar, but not identical, requirements and benefits.

Expedited development and review programs

In addition to the US orphan drug designation, Oxbryta received a Fast Track designation from the FDA for the potential treatment of SCD. The FDA's Fast Track program is intended to expedite or facilitate the process for reviewing new drugs that are intended to treat a serious or life threatening condition, where nonclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to both the product and the specific indication for which it is being studied.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval under Subpart H. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review. Our NDA for Oxbryta was reviewed by the FDA pursuant to priority review and received accelerated approval under Subpart H.

Additionally, Oxbryta also received a breakthrough therapy designation from the FDA for the potential treatment of SCD. The benefits of breakthrough therapy designation include the same benefits as a Fast Track designation, in addition to intensive guidance from the FDA to ensure an efficient drug development program. Fast Track designation, priority review, accelerated approval and breakthrough designation do not change the standards for approval but may expedite the development or approval process.

Pediatric information

Under the Pediatric Research Equity Act, or PREA, as amended, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration is required to submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or, if there is no end-of-Phase 2 meeting as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must

include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs. Generally, a drug product that has an indication for which orphan drug designation has been granted is exempt from the requirement to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients. Thus, our NDA for Oxbryta was not required to have this PREA assessment.

Post-marketing requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, monitoring and recordkeeping activities, submission of an NDA annual report, reporting of adverse experiences, product sampling and distribution requirements, and complying with complex promotion and advertising requirements, which include restrictions on promoting drugs for uses or for patient populations for which the drug was not approved (known as "off-label use"), and limitations on industry-sponsored scientific and educational activities and on interactions with healthcare providers. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with the first use of these materials, and may be required to be reviewed in advance in certain circumstances such as a new product launch, including for drugs such as Oxbryta that are approved pursuant to the FDA's Subpart H accelerated approval regulations. After 120 days following marketing approval, promotional materials for accelerated approval drugs must be submitted 30 days prior to use. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the pharmaceutical company may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require additional data or the conduct of additional nonclinical studies and clinical trials. Newly discovered or developed safety or effectiveness data may require changes to a drug's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures, including a Risk Evaluation and Mitigation Strategy, or REMS, or the conduct of post-marketing studies to assess a newly discovered safety issue. The FDA has authority to require post-market studies, in certain circumstances, on reduced effectiveness of a drug and the FDA may require labeling changes related to new reduced effectiveness information.

Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. The Drug Supply Chain Security Act, or DSCSA, was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. The law's requirements include the quarantine and prompt investigation of a suspect product, to determine if it is illegitimate, and notifying trading partners and the FDA of any illegitimate product. Drug manufacturers and their collaborators are also required to place a unique product identifier on prescription drug packages. This identifier consists of the National Drug Code, serial number, lot number and expiration date, in the form of a two dimensional data matrix barcode that can be read by humans and machines.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP requirements. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP requirements. Our third party

manufacturers must comply with cGMP requirements that require among other things, quality control and quality assurance, the maintenance of records and documentation, and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP requirements, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including recall.

Orange Book Listing

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A Section 505(b)(2) NDA is an application in which the applicant, in part, relies on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. Limited changes must be preapproved by the FDA via a suitability petition. ANDAs are termed “abbreviated” because they are generally not required to include nonclinical and clinical data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through *in vitro*, *in vivo*, or other testing. The generic version must deliver the same amount of active ingredients into a subject’s bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents having claims that cover the applicant’s product and method of use. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in Approved Drug Products with Therapeutic Equivalence Evaluations, also known as the Orange Book. These products may be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

Any applicant who files an ANDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must make patent certifications to the FDA relating to patents submitted to the FDA for the reference product: (1) that no patent information on the reference drug or method of use that is the subject of the application has been submitted to the FDA; (2) that any and all such patents submitted to the FDA have expired; (3) the date on which any such patent will expire and that ANDA approval will not be sought until after such patent expiration; or (4) that any such patent is invalid or will not be infringed upon by the manufacture, use, or sale of the drug product for which the ANDA is submitted. The last certification is known as a paragraph IV certification. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through a paragraph IV certification or if the applicant is not seeking approval of a patented method of use. If the applicant does not challenge the listed patents or does not indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired.

If the competitor has provided a paragraph IV certification to the FDA, the competitor must also send notice of the paragraph IV certification to the holder of the NDA for the reference listed drug and the patent owner

within 20 days after the application has been accepted for filing by the FDA. The NDA holder or patent owner may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a paragraph IV certification notice prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months from the date of the lawsuit, expiration of the patent, settlement of the lawsuit, a decision in the infringement case that is favorable to the applicant or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay.

In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owners regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation.

In connection with the NDA submission and approval of the NDA for Oxbryta, we have listed six patents in the Orange Book for Oxbryta.

United States patent term restoration and U.S. marketing exclusivity

Depending upon the timing, duration and specifics of the FDA approval of Oxbryta and any of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the patent term extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office, or USPTO, in consultation with the FDA, reviews and approves any application for patent term extension or restoration. Following the FDA approval of Oxbryta, we applied for restoration of patent term (also referred to as patent term extension) for Oxbryta.

Marketing exclusivity provisions under the FDCA provide a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator who holds the NDA for the active agent. The FDA has granted Oxbryta five-year marketing exclusivity, which will expire on November 25, 2024.

The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA for a drug product that contains an active moiety that has been previously approved if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use.

Five-year and three-year exclusivity will not delay the submission or approval of a full NDA by a competitor. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. Pediatric exclusivity is another type of regulatory market exclusivity in the United States which, if granted, adds six months to the end of existing exclusivity periods and patent terms, and may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued pre-approval written request for such a pediatric trial where information relating to the use of the product candidate in a pediatric population may produce health benefits in that population.

Federal, state and foreign healthcare laws, including anti-kickback, fraud and abuse and health information privacy and security laws

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, or HHS, the United States Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

Although we do not provide healthcare services, submit claims for third-party reimbursement, or receive payments directly from Medicare, Medicaid or other third-party payors for our products, we are subject to broadly applicable healthcare fraud and abuse regulation and enforcement by federal and state governments. Additionally, healthcare providers and third-party payors play a primary role in the recommendation of drugs and other medical items and services. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching hospitals and patient privacy laws and regulations and other healthcare laws.

Healthcare fraud and abuse and health information privacy and security laws potentially applicable to our operations include:

- the federal Anti-Kickback Law, which makes it illegal for any person to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, or in return for, that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus imprisonment and exclusion from government healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act, or FCA. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. This law applies to our marketing practices, educational programs, pricing policies and relationships with healthcare providers, by prohibiting, among other things, soliciting, receiving, offering or providing remuneration intended to induce the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare or Medicaid programs;
- federal civil and criminal false claims laws, including the FCA, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal

government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- federal "sunshine" requirements imposed by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, on drug, device, biological and medical supply manufacturers when payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS under the Open Payments Program, information regarding any payment or other "transfer of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in

civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;

- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- the Foreign Corrupt Practices Act, or FCPA, prohibits any United States individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party, or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts; and
- analogous state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws that require the licensure of sales representatives; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; data privacy and security laws and regulations in foreign jurisdictions that may be more stringent than those in the United States (such as the European Union, which adopted the General Data Protection Regulation, or GDPR, which became effective in May 2018); state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect; and state laws related to insurance fraud in the case of claims involving private insurers.

Additionally, pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the voluntary recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Regulations governing data collection and the use, processing and cross-border transfer of personal information

We have conducted, and expect to continue to conduct, clinical trials or continue to enroll subjects in our ongoing or future clinical trials in certain jurisdictions in which we may be subject to additional privacy

restrictions. Establishing an entity and operations in Europe also subjects us to additional privacy restrictions, including in relation to employee information. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which became effective in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR has increased our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will continue to be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's vote in favor of exiting the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information, and also regulates employee information. The CCPA went into effect in January 2020, and the California Attorney General has stated their office will commence enforcement actions against violators beginning in July 2020. While there is currently an exception for protected health information that is subject to HIPAA, as currently written, the CCPA will impact our business activities. The California Attorney General has proposed draft regulations, which have not been finalized to date, that may further impact our business activities if they are adopted. The uncertainty surrounding the implementation of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

European Union drug development, Orphan Drug and PRIME designations

In the EU, our product candidates may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory authorities has been obtained.

Similar to the United States, the various phases of nonclinical and clinical research in the EU are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new regulation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will apply following confirmation of full functionality of the Clinical Trials Information System, the centralized EU portal and database for clinical trials foreseen by the regulation, through an independent audit.

In November 2016, the EC, acting on a positive recommendation from the Committee for Orphan Medicinal Products, or COMP, of the EMA, designated Oxbryta as an orphan medicinal product for the treatment of SCD. Orphan drug status in the EU has similar, but not identical, requirements and benefits to US orphan drug status, including 10 years of marketing exclusivity from the approval of the marketing application, designated product-specific consultation by the EMA, and certain reductions or exemptions in regulatory fees.

In June 2017, the EMA granted PRIME designation for Oxbryta for the treatment of SCD. The PRIME program is a new regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need.

European Union drug review and approval

In the European Economic Area, or EEA, which is currently comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The Community MA is issued by the EC through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines, and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. This mandatory Centralized Procedure applies in the case of Oxbryta for SCD, in light of the 2016 designation of Oxbryta as an orphan medicinal product for the treatment of SCD.

The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging

proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above-described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

European Union new chemical entity exclusivity

In the EU, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with existing therapies.

European Union orphan designation and exclusivity

In the EU, the EC, after reviewing the opinion of the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU Community (or where it is unlikely that the development of the medicine would generate sufficient return to justify the investment) and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or, if a method exists, the product would be a significant benefit to those affected).

In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. In November 2016, we were granted orphan drug designation in the EU for Oxbryta for the potential treatment of SCD.

Rest of the world regulation

For other countries outside of the EU and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs (e.g., Medicare and Medicaid), commercial insurance and managed

healthcare organizations, as well as the level of reimbursement such third-party payors provide for our products. Patients and providers are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. In the United States, no uniform policy of coverage and reimbursement for drug products exists, and one payor's determination to provide coverage and adequate reimbursement for a product does not assure that other payors will make a similar determination. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. Many private payors, however, use coverage decisions and payment amounts determined by CMS as guidelines in setting their coverage and reimbursement policies. The coverage determination process is often time-consuming and costly and is likely to require us to provide scientific and clinical support for the use of our product candidates to each payor individually, with no assurance that coverage and adequate reimbursement will be obtained.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, and mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Effective in 2010, the ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, creating a new methodology by which rebates are calculated for drugs that are inhaled, infused, instilled, implanted or injected, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits (phased-in by 2014). Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Parts A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment

limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of Oxbryta or our product candidates, if any such drug or the condition that they are intended to treat are the subject of such research. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of Oxbryta or our product candidates. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment or utilization may not be sufficient to allow us to sell our drugs on a profitable basis.

In recent years, additional laws have resulted in direct or indirect reimbursement reductions for certain Medicare providers, including:

- The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2029 unless additional Congressional action is taken.
- The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. We expect that an increasing emphasis on cost containment measures in the United States will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products, for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved.

U.S. Healthcare Reform and regulatory changes

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could affect our ability to profitably sell our products. In the United States, there have been and continue to be laws enacted by the federal government, state governments, regulators and third-party payers to control healthcare costs, and generally, to reform the healthcare system in the United States. For example, the ACA was passed in March 2010 and has substantially changed the way healthcare is delivered and financed by both governmental and private insurers. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. The required discount was increased to 70% on January 1, 2019 pursuant to subsequent legislation.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. The full impact of the ACA, any law repealing, replacing, or modifying elements of it, and the political uncertainty surrounding its repeal, replacement, or modification on our business remains unclear. We expect that additional federal healthcare reform measures may be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare drugs and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability and may increase our regulatory burdens and operating costs.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices, including for specialty drugs. For example, there have been several recent federal Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. HHS has already started the process of soliciting feedback on some of these

measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning in January 2020, codifying an earlier CMS policy change. Although a number of these, and other proposed measures may require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Finally, in May 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Employees

As of December 31, 2019, we employed 352 full-time employees, including 156 in research and development and 196 in selling, general and administrative, which includes our commercial team, in the United States. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

Research and Development

Research and development expenses were $174.6 million for the year ended December 31, 2019, $131.3 million for the year ended December 31, 2018 and $87.8 million for the year ended December 31, 2017.

Financial Information about Segments

We operate in a single accounting segment—dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders. Refer to Note 1, “Organization and Basis of Presentation” in the Notes to Consolidated Financial Statements included elsewhere in this report.

Corporate Information

We were incorporated in Delaware in February 2011 and commenced operations in May 2012. Our principal executive offices are located at 171 Oyster Point Blvd., Suite 300, South San Francisco, California 94080. Our telephone number is (650) 741-7700 and our e-mail address is investor@gbt.com. Our Internet website address is www.gbt.com. No portion of our website is incorporated by reference into this Annual Report on Form 10-K.

You are advised to read this Annual Report on Form 10-K in conjunction with other reports and documents that we file from time to time with the Securities and Exchange Commission, or SEC. In particular, please read our Quarterly Reports on Form 10-Q and any Current Reports on Form 8-K that we may file from time to time. You may obtain copies of these reports directly from us or from the SEC. In addition, the SEC maintains information for electronic filers (including Global Blood Therapeutics, Inc.) at its website at www.sec.gov. We make our periodic and current reports available on our internet website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

Item 1A. *Risk Factors*

This Annual Report on Form 10-K contains forward-looking information based on our current expectations. Because our business is subject to many risks and our actual results may differ materially from any forward-looking statements made by or on behalf of us, this section includes a discussion of important factors that could affect our business, operating results, financial condition and the trading price of our common stock. You should carefully consider these risk factors, together with all of the other information included in this Annual Report on Form 10-K as well as our other publicly available filings with the SEC.

Risks Related to Commercialization

Our business is substantially dependent on our ability to successfully commercialize Oxbryta, and the commercial success of Oxbryta or any future drug we may develop or obtain will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community and marketplace.

Our business depends heavily on our ability to successfully commercialize our first approved product, Oxbryta, for the treatment of sickle cell disease, or SCD. Oxbryta or any future drug of ours approved for commercial sale may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community and marketplace. If Oxbryta or any other approved drug does not achieve an adequate level of acceptance, we may not generate significant revenue from drug sales and we may not become profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that the drug, in addition to treating the target indication, also provides incremental health benefits to patients. For example, there have been numerous instances of government and private payors placing restrictions on coverage for products approved by the U.S. Food and Drug Administration, or FDA, under the FDA's Subpart H regulations, or Subpart H, so even though the FDA granted Oxbryta accelerated approval, healthcare payors may place restrictions on coverage for Oxbryta because of its accelerated approval status, labeling limitations or other factors. Our efforts to educate the medical community and third-party payors about the benefits of Oxbryta or any future drug approved for commercial sale will require significant resources and may never be successful. The degree of market acceptance of Oxbryta and any other approved drugs that we may pursue will depend on a wide range of factors, including:

- the demonstrated efficacy and potential advantages of our drugs compared to alternative treatments;
- our ability to offer our drugs for sale at competitive prices;
- the availability of third-party coverage and adequate reimbursement;
- the convenience and ease of administration of our drugs compared to alternative current and future treatments;
- the willingness of the SCD or other target patient populations to try new therapies and of physicians to prescribe these therapies;
- the availability of our drugs and our ability to meet market demand, including a reliable supply for long-term chronic treatment;
- the strength of labeling, marketing and distribution support;
- the clinical indications and approved labeling for which the drug is approved, including labeling restrictions for drugs approved under Subpart H, such as Oxbryta;
- the prevalence and severity of any side effects and overall safety profile of the drug; and
- any restrictions on the use of the drug, including together with other medications.

If our sales and marketing capabilities for Oxbryta are not effective, or we are unable to establish or secure effective sales and marketing capabilities for any future drug approved for commercial sale, we may be unsuccessful in our commercial efforts.

In 2019, we established the infrastructure we believe is adequate for the commercial launch of Oxbryta in the United States, which occurred in December 2019. This included establishing a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize Oxbryta in the United States. Our commercialization of Oxbryta in the United States will continue to be expensive, difficult, risky and time consuming, and we may not deploy or have adequate resources over time to support the successful commercialization of Oxbryta. Any failures or delays in our commercial efforts, including with respect to any changes in related resources or activities following launch, could adversely impact the commercialization of Oxbryta or any other products, if any are approved.

Although many of our employees have experience with commercializing products while employed at other companies, our 2019 launch of Oxbryta is our first experience marketing and selling a drug together as a management team. To successfully commercialize Oxbryta or any other drugs we may develop or obtain, we will need to continue to develop and strengthen our commercial capabilities, either on our own or with others. Our initial estimate of the size of the required sales force may be materially more or less than the size of the sales force actually required to effectively commercialize Oxbryta or any other product candidates, if any. For example, we may have hired substantially more sales representatives than required and may incur excess costs as a result.

Another potential challenge for our commercial efforts is frequency of doctor visits by SCD patients. In the United States, fewer than 10% of Medicaid and Medicare patients living with SCD see a hematologist at least once per year and approximately 20% of SCD patients receive most of their care in the emergency room. This infrequency of doctor visits may impede prescriptions for Oxbryta.

With respect to certain geographical markets, we may seek to enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize Oxbryta or future drugs, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. For example, in November 2019, the FDA approved Novartis' biologic, crizanlizumab for the treatment of patients with SCD, and Novartis also announced that they have submitted crizanlizumab for a conditional approval by the European Medicines Agency, or EMA, for potential approval in the third quarter of 2020 for the treatment of SCD. Without an effective internal team or the support of a third party to perform marketing and sales functions, we would be unable to compete successfully against more established companies, and our commercial efforts and ability to generate revenues would be impaired.

Our profitability will depend significantly on our ability to sell sufficient amounts of product at competitive prices and on the availability of adequate coverage and reimbursement through governmental or private third-party payors. The insurance coverage and reimbursement status of newly approved products is uncertain in the United States and elsewhere, and failure to obtain or maintain adequate coverage and reimbursement for Oxbryta or any other products we may develop due to price controls, resource constraints or reimbursement limitations could limit our ability to market those products and impair our ability to generate revenue.

Our target patient populations are small, and, accordingly, the pricing, coverage and reimbursement of Oxbryta or any of our product candidates, if approved, must be adequate to support our commercial infrastructure. To achieve profitability, our per-patient prices must be sufficient to recover our development and manufacturing costs, and we must be able to sell sufficient amounts of product at these prices. Additionally, the availability of government funded or private insurance coverage for Oxbryta and any other product candidates for

any approved indications, if any, and the extent of reimbursement by governmental and private payors, will be essential for most patients to be able to afford Oxbryta or any of our other specialty products, if approved. In particular, the list price for Oxbryta in the United States is $125,000 per year, and a significant percentage of patients with SCD in the United States rely on government programs, such as Medicare and Medicaid, for their coverage of drugs and other medical care, so the availability of federal and state coverage of Oxbryta is critical to the success of our commercialization efforts for Oxbryta in the United States. Sales of Oxbryta or any future drug we may develop or obtain will depend substantially, both domestically and abroad, on the extent to which the costs of such drugs will be paid by third party payors, like private health insurers, including health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, and government health administration programs. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize Oxbryta or any future drug we may develop or obtain. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved drug products, and even more uncertainty related to the insurance coverage for products, such as Oxbryta, that receive accelerated approval by the FDA under Subpart H (including in the period before required post-marketing confirmatory studies to verify clinical benefit). The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. For example, the payor's reimbursement payment rate may not be adequate or may require co-payments that patients find unacceptably high. Additionally, coverage and reimbursement for products can differ significantly from payor to payor.

In the United States, significant decisions about reimbursement for new medicines are made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare, and federal and state programs enter into contracts with drug manufacturers for discounted drug prices for Medicare, VA/Federal Supply Schedule, 340B and Medicaid under the Medicaid Drug Rebate Program, among others. The practices and requirements relating to these arrangements are highly complex and subject to differing regulatory requirements and time frames, which will impact the commercialization of Oxbryta. For example, payment of rebates by drug manufacturers for Medicaid purchases are determined by each state, and in some cases, if a company does not enter into a rebate agreement, its Medicaid sales will be subjected to a "prior authorization" procedure that requires state agency approval to qualify a doctor's prescription for reimbursement. Limitations could also come from entities such as local Medicare carriers, fiscal intermediaries, or Medicare Administrative Contractors. Further, Medicare Part D, which provides a pharmacy benefit to certain Medicare patients, does not require participating prescription drug plans to cover all drugs within a class of products. Our business could be materially adversely affected if private or governmental payors, including Medicare Part D prescription drug plans, were to limit access to, or deny or limit reimbursement of, Oxbryta or any of our product candidates, if approved.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the potential pricing and usage of Oxbryta and any future drugs we may develop or obtain. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems, and changes to these regulations over time contribute to uncertainty regarding the ability to obtain pricing and usage approvals for our product candidates outside of the United States. In addition, the prices of medicines under such systems are, in general, substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing

regulation could restrict the amount that we are able to charge for our product candidates outside of the United States. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

In many non-U.S. jurisdictions, including some countries in the European Union, the proposed pricing for a drug must be approved before it may be lawfully marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted and reimbursement may in some cases be unavailable. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. The requirements governing drug pricing vary widely from country to country and products may be subject to continuing governmental control following approval. For example, reimbursement in the European Union must be negotiated on a country-by-country basis and, in many countries, the product cannot be commercially launched until reimbursement is approved. Furthermore, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use, including by approving a specific price for the medicinal product or adopting a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In addition, to obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, or to meet other criteria for pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products or product candidates.

Moreover, increasing efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and levels of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for Oxbryta or our product candidates. We expect to experience pricing pressures in connection with the sale of Oxbryta and any future drugs we may develop or obtain, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative and political changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. For example, third-party payors are increasingly requiring higher levels of evidence of the benefits and clinical outcomes of new technologies, benchmarking against other therapies, seeking performance-based discounts, and challenging the prices charged. We cannot be sure that coverage will be available for Oxbryta or any other product we commercialize and, if available, that the reimbursement rates will be adequate, as increasingly high barriers are being erected to the entry of new products. In addition, drug prices are under significant scrutiny in the markets in which our products are or may be sold, and drug pricing and other healthcare costs continue to be subject to intense political and social pressures that we anticipate will continue and escalate on a global basis.

Our future profitability will depend, in part, on our ability to commercialize and obtain reimbursement for Oxbryta and our product candidates in markets within and outside of the United States and Europe. If reimbursement for Oxbryta, or our product candidates, if approved, is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, in the United States or, based on the large population of patients with SCD who reside in foreign countries, abroad, our business and operations may be harmed, our stock price may be adversely impacted and experience periods of volatility, we may have difficulty raising funds and our results of operations may be adversely impacted.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

If we commercialize Oxbryta and any future drugs we may develop or obtain in foreign markets, we would be subject to additional risks and uncertainties, including:

- the burden of complying with complex and changing foreign regulatory, tax, accounting, compliance and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of bioequivalent or generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations;
- potential resource constraints, including with respect to patients' ability to obtain reimbursement for our products in foreign markets; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Any of these factors could impair our ability to commercialize Oxbryta and any future drugs we may develop or obtain outside the United States, which could have a material adverse effect on our business and results of operations.

With the FDA approval of Oxbryta, and with respect to any other product candidate that receives regulatory approval, we will be subject to ongoing regulatory obligations and scrutiny, which may include significant restrictions relating to product labeling, distribution or other post-marketing requirements.

Even if a product candidate is approved, regulatory authorities may still impose significant restrictions on its indicated uses, approved labeling, distribution or marketing or may impose ongoing requirements for potentially costly post-marketing studies. For example, because the FDA approved Oxbryta under the accelerated approval pathway under Subpart H, we must conduct at least one post-marketing confirmatory study to verify clinical risk/benefit, which we intend to satisfy through our recently initiated HOPE-KIDS 2 Study, and we may not be able to successfully and timely complete this study or any other post-marketing confirmatory study as required to maintain approval or achieve full approval. Also, the FDA has restricted the indicated use of Oxbryta under the approved label to patients 12 years and older. While we plan to conduct additional studies to potentially lower the indicated age range down to 9 months of age, failure to reach agreement with the FDA on these studies, failure to obtain adequate results from them, or disagreements with regulatory authorities over the interpretation of the results may prevent expansion of the age range within our approved label.

Furthermore, any new legislation addressing drug safety or other drug related issues could result in delays or increased costs to assure compliance. With respect to Oxbryta and any other product candidate that is approved, at a minimum, they will each be subject to current standard ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, including both federal and state requirements in the United States. In addition, regulatory agencies may not approve labeling claims that are necessary or desirable for the successful commercialization of Oxbryta, inclacumab or any other product candidates. For example, the development of Oxbryta for the prophylactic treatment of SCD in pediatric patients is an important part of our current business strategy, and if we are unable to obtain regulatory approval for Oxbryta for the desired age ranges or other key labeling parameters, our business is likely to suffer.

In addition, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices, or cGMPs. For Oxbryta, inclacumab and any other product candidates we may pursue, we are wholly reliant on third party contract manufacturers for clinical as well as any commercial supplies of product candidates and products. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMP requirements and must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. We are also required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities, and to comply with requirements concerning advertising and promotion for Oxbryta and any future products. In addition, we are subject to very rapid reporting obligations relating to any adverse events or serious adverse events relating to Oxbryta and our product candidates. Our failure to report adverse events we become aware of within the prescribed timeframes could have serious negative consequences for our commercialization, development programs, business and operations. In addition, any promotional communications or materials for prescription drugs are subject to a variety of complex legal and regulatory restrictions, including, but not limited to, consistency with the approved product's approved label. Failure to obey these standard marketing requirements for Oxbryta or any other approved product, if any, could have serious negative consequences for our commercialization activities, business and operations.

If the FDA or any comparable foreign regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with a sponsor's activities relating to the promotion, marketing, or labeling of a product, these regulatory agencies may impose restrictions or sanctions on that product or us, including requiring withdrawal of the product from the market. In addition, in the United States, a wide range of commercialization and pre-launch activities relating to a drug candidate are subject to potential for significant civil and/or criminal liability and sanctions under federal anti-kickback and fraud and abuse statutes and regulations. If we fail to comply with any of these complex applicable regulatory requirements, a regulatory agency or enforcement authority may:

- issue untitled or warning letters;
- impose civil or criminal penalties;
- impose injunctions;
- impose fines;
- impose additional specialized restrictions on the company's activities and practices;
- suspend regulatory approval;
- suspend ongoing clinical trials;
- seek voluntary product recalls and impose publicity requirements;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products.

As a company, we have limited experience with obtaining approval for, launching or commercializing any product candidates or products, or with complying with most of these complex ongoing regulatory requirements. It will continue to take significant effort and management attention to address compliance with these requirements with respect to Oxbryta in the United States and in any jurisdiction for which we seek to commercialize Oxbryta or any other product candidate, if approved. Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity even if significant liabilities do not result. Any failure to comply with these complex ongoing

regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from Oxbryta or to obtain approval for, launch, commercialize and generate revenues from inclacumab or any future product candidates. If we are subject to regulatory sanctions or if regulatory approval for our product candidates is withdrawn or limited, our business, prospects, financial condition and results of operations would be significantly harmed.

Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers are or will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Our current and future operations are or will be directly, or indirectly through our prescribers, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations. These laws may impact, among other things, our current business operations, including our sales, marketing, distribution, commercialization, medical and educational programs and our clinical research activities, and they may constrain our business and financial arrangements and relationships with healthcare providers, physicians and other parties through which we market, sell and distribute Oxbryta and any future drugs we may develop or obtain. We may also be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include the federal Anti-Kickback Statute, the federal False Claims laws, the U.S. Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, the Physician Payment Sunshine Act, and analogous state laws and regulations such as state anti-kickback and false claims laws and analogous non-U.S. fraud and abuse laws and regulations, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors.

Ensuring that our business activities (including our operations and arrangements with third parties) comply with applicable healthcare laws and regulations is complex, time-consuming, costly and could materially impact our operations. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse, price reporting or other healthcare laws and regulations.

Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these requirements, these risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal, state and foreign privacy, security, and fraud requirements is costly. Any action against us for violation of these requirements, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management’s attention from our business and operation, and could negatively impact the price of our common stock.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform and other factors. Federal and state enforcement bodies in the United States regularly pursue a large number of investigations, prosecutions, convictions and settlements in the healthcare industry, and in the European Union GDPR enforcement is increasing. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion of products or individuals from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to

resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable requirements, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could restrict or regulate post-approval activities, affect our ability to profitably sell Oxbryta and any other drug candidates for which we obtain marketing approval, and prevent or delay marketing approval of our drug candidates. For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act or ACA, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry.

Since its enactment, there have been many judicial, President, and Congressional challenges to numerous aspects of the ACA.

The full impact on our business of the ACA, the potential impacts of any challenges, including any laws repealing and/or replacing elements of it, as well as the political uncertainty surrounding any repeal or replacement legislation, remain unclear.

Additionally, at the federal level, statutes and regulations routinely impact a variety of parameters relating to federal programs and Medicaid. For example, CMS's final rule regarding the Medicaid drug rebate program, issued in 2016, revised the manner in which the "average manufacturer price" is to be calculated by manufacturers participating in the program. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. The full impact of these federal and state laws and regulations, as well as other new laws and reform measures that may be proposed and adopted in the future, remains uncertain, but may result in additional reductions in Medicaid and other health care funding, or higher production costs which could have a material adverse effect on our customers and, accordingly, our financial operations.

There have been multiple recent U.S. congressional inquiries and proposed and adopted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs and biologics. In addition, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current U.S. presidential administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional

health care authorities are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for Oxbryta and our drug candidates, once approved, or put pressure on our product pricing over time.

Moreover, there have been a number of other legislative and regulatory changes in recent years aimed at the biopharmaceutical industry. For instance, the Drug Quality and Security Act imposes obligations on manufacturers of biopharmaceutical products related to product tracking and tracing. Among the requirements of this legislation, manufacturers are required to provide certain information regarding the product to individuals and entities to which product ownership is transferred, will be required to label products with a product identifier, and are required keep certain records regarding the product. The transfer of information to subsequent product owners by manufacturers will eventually be required to be done electronically. Manufacturers are also required to verify that purchasers of the manufacturers' products are appropriately licensed. Further, manufacturers have product investigation, quarantine, disposition, and FDA and trading partner notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products that would result in serious adverse health consequences or death to humans, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

We expect federal and state healthcare reform measures that may be adopted in the future in the United States may result in more rigorous coverage criteria, increased regulatory burdens and operating costs, decreased net revenue from our pharmaceutical products and additional downward pressure on the price that we receive for Oxbryta and any of our drug candidates approved for use. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. These legislative and executive efforts have significantly increased uncertainty regarding the availability of healthcare programs, insurance coverage and reimbursement as a general matter as well as for Oxbryta and our product candidates, and we cannot predict how these events will impact our business or operations. Accordingly, at this time it is difficult to determine the full impact of these efforts on our business. In the United States many patients with SCD participate in the Medicaid program, and the impact of uncertainty or changes relating to the ACA or healthcare programs, insurance coverage or reimbursement generally have a particularly significant impact on our business or results of operations.

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize Oxbryta and our product candidates.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies and development candidates that are or may compete with Oxbryta and inclacumab for the potential treatment of SCD. For example, the FDA approved Novartis' crizanlizumab in November 2019. Both crizanlizumab and inclacumab are human monoclonal antibodies against p-selectin for the treatment of vaso-occlusive crises, or VOC, in patients with SCD. The FDA's approval of crizanlizumab results in another new and innovative SCD product entering the United States SCD market approximately one week earlier than Oxbryta, and substantially earlier than any potential approval of our inclacumab product candidate (which could be a direct competitor to crizanlizumab). As a result, the commercialization of crizanlizumab may also impact our commercialization of Oxbryta in the United States, as well as inclacumab if we are successful in developing and obtaining approval for it for SCD patients. In addition, Novartis has announced a conditional EMA approval application for a potential conditional approval of crizanlizumab in the third quarter of 2020.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Many of our

competitors have substantially greater financial, technical, and other resources, such as larger research and development, marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization and market penetration than we do. Additionally, technologies developed by our competitors may render Oxbryta or our product candidates uneconomical or obsolete, and we may not be successful in marketing any drugs or product candidates against competitors.

If the market opportunities for Oxbryta or our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Our ability to successfully identify patients and acquire a significant market share will be necessary for us to achieve profitability and growth.

Our initial development and commercialization efforts are focused on the potential of Oxbryta to treat SCD. Our projections of both the number of people who have SCD, as well as the subset of people with SCD who have the potential to benefit from treatment with Oxbryta, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of SCD. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for Oxbryta and our product candidates may be limited or may not be amenable to treatment with Oxbryta or our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Restrictions on labeling of any approved product, including any restrictions that may be imposed in connection with any approval under Subpart H, may also limit the size of the potential market for Oxbryta and our product candidates. Further, even if we obtain significant market share for Oxbryta or any other drug we may develop or obtain, because the potential target populations are small, we may never achieve profitability despite obtaining such significant market share.

Risks Related to Our Financial Position and Need for Additional Capital

We are a biopharmaceutical company with only one drug approved for marketing in the United States and with a limited operating history. We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We have generated limited revenue since our inception, which, together with our limited operating history, may make it difficult for you to assess our future viability.

We are a biopharmaceutical company with only one drug, Oxbryta, approved for marketing, and such approval is only for the United States. We also have a limited operating history upon which you can evaluate our business and prospects. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused principally on developing Oxbryta, and our current clinical development activities are focused on Oxbryta and inclacumab. In August 2018, we entered into an exclusive worldwide license agreement with F. Hoffman-LaRoche and Hoffman-La Roche Inc., collectively, Roche, for the development and commercialization of inclacumab.

We are not profitable and have incurred losses in each year since our inception in February 2011 and the commencement of our principal operations in May 2012. Our net losses for the years ended December 31, 2019

and 2018 were $266.8 million and $174.2 million, respectively. As of December 31, 2019, we had an accumulated deficit of $738.9 million. We have only recently begun to generate revenues with the December 2019 commercial launch of Oxbryta, and have financed our operations primarily through the sale of equity securities. We continue to incur significant research and development and other expenses related to our ongoing operations and expect to incur losses for the foreseeable future. We anticipate these losses will increase as we:

- commercialize Oxbryta and continue related clinical development, including winding down our recently completed Phase 3 HOPE Study and conducting (i) our ongoing Phase 2a HOPE-KIDS 1 Study of Oxbryta, (ii) our recently initiated HOPE-KIDS 2 Study, which we intend to serve as our post-confirmatory study of Oxbryta in SCD (and any other post-marketing studies that may be required by regulatory authorities, if any), and (iii) any additional clinical trials of Oxbryta we may conduct now or in the future in SCD patients or for any other indications for Oxbryta, inclacumab or any other product candidates, if any;
- establish and maintain manufacturing and supply relationships with third parties that can provide adequate supplies (in amount and quality) of Oxbryta and inclacumab to support commercialization and further clinical development;
- seek and obtain additional regulatory and marketing approvals for Oxbryta for SCD, including for younger pediatric patient populations, or any potential approvals we may pursue;
- maintain a sales and marketing organization and enter into selected collaborations to commercialize Oxbryta for SCD or any other approved indication;
- maintain a medical affairs organization to advance our engagement with healthcare providers and stakeholders;
- advance our other programs, including inclacumab, through nonclinical and clinical development and commence development activities for any additional product candidates we may identify and pursue; and
- expand our organization to support our commercialization, research, development and medical activities and our operations as a public company.

Prior to the December 2019 commercial launch of Oxbryta, we had never generated any revenues from product sales, and we may never be able to achieve significant revenues or profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to maintain adequate cash reserves to commercialize Oxbryta, advance our development programs or achieve approval to commercialize any other products, or our failure to achieve sustained profitability, would depress the value of our company and could impair our ability to raise capital, expand our business, market Oxbryta, diversify our research and development pipeline, market any other product candidates we may identify and pursue (if approved), or continue our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We may require substantial additional funds to achieve our business goals. If we are unable to obtain such funds when needed and on acceptable terms, we could be forced to delay, limit or terminate our commercialization activities for Oxbryta, our product development efforts or other operations. Raising additional capital may subject us to unfavorable terms, cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to Oxbryta, our product candidates or technologies.

We are currently commercializing Oxbryta and investigating Oxbryta in clinical development to support its potential full approval by the FDA and opportunities for potential label expansion. We are evaluating the safety and pharmacokinetics of single and multiple doses of Oxbryta in our HOPE-KIDS 1 Study, a Phase 2a clinical trial in adolescent and pediatric patients with SCD, which we expanded to include a new single-dose cohort in children aged 6-11. Our clinical program for Oxbryta also includes multi-national open label extension, or OLE,

clinical studies for adult and pediatric patients in HOPE Study countries who have completed participation in the ongoing Phase 3 HOPE Study and elect to continue to receive Oxbryta. We have initiated our HOPE-KIDS 2 Study, which is our TCD post-confirmatory study of Oxbryta in SCD (to potentially satisfy the FDA's requirement for a post-confirmatory study under Subpart H). Oxbryta is currently our only compound in clinical development, although we are conducting nonclinical research activities in other programs.

Discovering, developing and commercializing biopharmaceutical products is expensive and time-consuming, and we expect our selling, general and administrative and research and development expenses to increase substantially in connection with our ongoing activities, particularly as we continue to commercialize Oxbryta and engage in research and development efforts for Oxbryta, inclacumab and other product candidates that we may identify and pursue in clinical trials. As of December 31, 2019 and 2018, we had working capital of $556.5 million and $452.0 million, respectively, and capital resources consisting of cash and cash equivalents and short and long-term marketable securities totaling $695.0 million and $591.8 million, respectively. We expect that our existing capital resources consisting of cash and cash equivalents and marketable securities will be sufficient to fund our operations for at least the next twelve months. Because the outcome of commercialization, reimbursement and any clinical development and regulatory approval process is highly uncertain, we cannot reasonably estimate the actual capital amounts necessary to successfully commercialize Oxbryta and complete our ongoing and planned additional development of activities for Oxbryta or any other future product candidates.

Our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations or license and development agreements. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize Oxbryta, inclacumab or any other product candidates that we may identify and pursue. Moreover, such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future funding requirements will depend on many factors, including, but not limited to:

- our ability to successfully commercialize Oxbryta, inclacumab and any other product candidates we may identify and develop in any territories;
- the manufacturing, selling, and marketing costs associated with the commercialization of Oxbryta and the potential commercialization of inclacumab and any other product candidates we may identify and develop, including the cost and timing of establishing or maintaining our sales and marketing capabilities in any territory(ies);
- the amount and timing of sales and other revenues from Oxbryta, inclacumab and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the time and cost necessary to wind down our completed Phase 3 HOPE Study, to conduct and complete multiple ongoing studies (including our HOPE-KIDS 1 Study, Phase 3 HOPE-KIDS 2 Study and our OLE study in HOPE study countries;
- the time and cost necessary to conduct and complete any additional clinical studies required to pursue additional regulatory approvals for Oxbryta for SCD, including our recently initiated Phase 3 HOPE-KIDS 2 Study (which is necessary to move from our current Subpart H approval to a full approval) and any studies to support potential label expansions into younger SCD pediatric populations, or any other post-marketing studies for Oxbryta for SCD;
- the progress, data and results of clinical trials of Oxbryta;

- the progress, timing, scope and costs of our nonclinical studies, our clinical trials and other related activities, including our ability to enroll subjects in a timely manner for our ongoing and future clinical trials of Oxbryta, inclacumab or any other product candidate that we may identify and develop;
- the costs of obtaining clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates we may identify and develop;
- our ability to advance our development programs, including for Oxbryta, inclacumab and any other potential product candidate programs we may identify and pursue, the timing and scope of these development activities, and the availability of approval for any of our other product candidates;
- our ability to successfully obtain any additional regulatory approvals from any regulatory authorities, and the scope of any such regulatory approvals, to market and sell Oxbryta, inclacumab and any other product candidates we may identify and develop in any territory(ies);
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies, and the costs and timing associated with any such acquisitions or in-licenses;
- our ability to attract, hire, and retain qualified personnel; and
- the costs of maintaining, expanding, and protecting our intellectual property portfolio.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit or terminate our development or commercialization activities for Oxbryta, inclacumab or for any other product candidates we may identify and pursue, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially and adversely affect our business, prospects, financial condition and results of operations.

We are party to a loan and security agreement that contains operating and financial covenants that may restrict our business and financing activities.

In December 2019, we entered into a loan agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent and a lender, and Biopharma Credit Investments V (Master) LP, as a lender, for a senior secured credit facility consisting of an initial term loan of $75.0 million, with an option to draw an additional $75.0 million until December 31, 2020. Borrowings under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

The Term Loan restricts our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business or property, subject to limited exceptions;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;
- incur additional indebtedness or create encumbrances on our assets;
- pay dividends, other than dividends paid solely in shares of our common stock, or make distributions on and, in certain cases, repurchase our stock;
- repay subordinated indebtedness; or
- make certain investments.

In addition, we are required under the Term Loan to comply with various operating covenants and default clauses that may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies. A breach of any of these covenants or clauses could result in a default under the Term Loan, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable.

If we are unable to generate sufficient cash to repay our debt obligations when they become due and payable, we may not be able to obtain additional debt or equity financing on favorable terms, if at all, which may negatively affect our business operations and financial condition.

Risks Related to Our Business and the Clinical Development, Regulatory Review and Approval of Our Product Candidates

If we are unable to obtain regulatory approval in additional jurisdictions for Oxbryta or one or more jurisdictions for inclacumab or any future product candidates that we may identify and develop, our business will be substantially harmed.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Approval by the FDA and comparable foreign regulatory authorities is lengthy and unpredictable and depends upon numerous factors. Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. We have only obtained regulatory approval for Oxbryta in the United States, and it is possible that inclacumab or any other product candidates we may seek to develop in the future will never obtain any regulatory approval.

Applications for product candidates could fail to receive regulatory approval for many reasons, including, but not limited to:

- we may not be able to demonstrate to the satisfaction of regulatory authorities (including the EMA) that Oxbryta, inclacumab or any other product candidates we may develop are safe and effective for any proposed indications;
- the FDA or comparable foreign regulatory authorities may disagree with our plans or expectations regarding the pathways and endpoints for approval, including the availability of accelerated approval, or the design or implementation of our nonclinical studies or clinical trials;
- the populations studied in our clinical programs may not be sufficiently broad or representative to assure safety or demonstrate efficacy in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may require additional nonclinical studies or clinical trials beyond those we anticipate;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data and results from our nonclinical studies or clinical trials;
- the data and results collected from nonclinical studies or clinical trials of Oxbryta, inclacumab and any other product candidates that we may identify and pursue may not be sufficient to support the submission for regulatory approval;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract and rely on for all clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates (if any); and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change in a manner that renders our development or manufacturing efforts insufficient for approval.

The lengthy regulatory review and approval process, as well as the inherent unpredictability of the results of nonclinical studies and clinical trials, and our reliance on third-party manufacturers for any product candidates, may result in our failure to obtain regulatory approval to market Oxbryta outside of the United States or to market inclacumab or other product candidates that we may pursue in the United States or elsewhere, which would significantly harm our business, prospects, financial condition and results of operations.

Expedited development and regulatory approval programs for Oxbryta, such as the accelerated approval under Subpart H, may not lead to a faster development or regulatory review or approval process, may not lead to any approval, and may lead to an approval that is later withdrawn.

The FDA approved Oxbryta through the accelerated approval process under Subpart H, and we believe there may be an opportunity to accelerate the development and regulatory approval process for Oxbryta through the EMA's PRIME program. While the FDA approved Oxbryta under Subpart H, we cannot be assured that any other product candidates that we may develop will qualify for or benefit from any such expedited programs in the United States, including under Subpart H, or, with respect to Oxbryta and any other product candidates, any foreign regulatory jurisdictions (including the EMA's PRIME program).

In June 2017, the EMA granted PRIME designation for Oxbryta for the treatment of SCD. The PRIME program is a regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need.

The FDA grants accelerated approval under Subpart H for new drugs that address serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments. Under Subpart H, the FDA may grant marketing approval for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity.

Drugs approved under Subpart H are required to be further evaluated in at least one post-marketing study to verify clinical benefit. To satisfy such requirement, we have initiated our TCD post-confirmatory study, HOPE-KIDS 2 Study. We previously announced that the FDA agreed that TCD flow velocity would be an acceptable primary endpoint in a post-approval confirmatory study of Oxbryta to demonstrate stroke risk reduction for purposes of full approval by the FDA and that we had reached final agreement with the FDA on the design of the TCD post-confirmatory study.

We may not be able to complete our HOPE-KIDS 2 Study or any other successful post-marketing confirmatory study as required to maintain approval and achieve full approval, or data and results from our required post-marketing confirmatory program may not verify Oxbryta's clinical benefit to maintain approval and achieve full approval, in which case the product may be required to be withdrawn from market approval.

Access to any expedited program, including through the FDA (such as accelerated approval under Subpart H), may be withdrawn by the FDA or a foreign regulatory authority if it believes that the program is no longer supported by data from our clinical development, and accelerated approval under Subpart H may be withdrawn if, among other reasons, required post-marketing confirmatory studies are not completed or if the FDA determines the results of post-marketing confirmatory studies do not verify clinical benefit.

All of our programs other than Oxbryta are still in earlier development stages, so we remain very reliant on the potential success of Oxbryta in the clinic and in the marketplace. If we are unable to successfully commercialize Oxbryta for SCD or complete clinical development of Oxbryta, or experience delays in doing so, our business will be materially harmed.

To date, we have invested a majority of our efforts and financial resources in the nonclinical and clinical development of Oxbryta, including conducting nonclinical studies and clinical trials, submitting and obtaining approval for an NDA, and providing general and administrative support for these operations. We do not have any other clinical product candidates at this time, and our only clinical development program for Oxbryta is in SCD. Our future success is highly dependent on our ability to successfully continue to develop, obtain and maintain regulatory approval for, and commercialize Oxbryta inside and outside the United States for SCD.

We are currently evaluating Oxbryta in SCD patients in our ongoing HOPE-KIDS 1 Study, our recently initiated HOPE-KIDS 2 Study (which is our post-approval confirmatory study), and other ongoing and planned clinical trials, as we wind down our recently completed HOPE Study. We are also generating additional clinical data regarding Oxbryta in SCD patients in our OLE studies for HOPE Study sites in multiple countries.

All of our other programs are in earlier stages of research and development, and we have no other product candidates in clinical trials other than Oxbryta. As a result, even after in-licensing the inclacumab program, we are very dependent on Oxbryta for our business, prospects, financial condition and results of operations.

We are also very dependent on the data and results that we obtain over time from our clinical program for Oxbryta, including our post-approval confirmatory, HOPE-KIDS 2 Study. The primary endpoint of the HOPE-KIDS 2 Study relates to TCD measurement, and we have not previously conducted any Phase 3 clinical study of Oxbryta in SCD patients using this primary endpoint, and we do not believe this measure has been used as a primary endpoint for any registration studies for any other SCD therapies.

As we continue our clinical development of Oxbryta, the additional data we generate could be different from, including less favorable in terms of efficacy and/or safety, than the data generated and discussed with the FDA to date. If this were to occur, it could significantly impact our continued development and commercialization of Oxbryta. In addition, depending on the results we obtain from our recently initiated HOPE-KIDS 2 Study, which we intend to be satisfy our post-approval confirmatory requirement under Subpart H, accelerated approval of Oxbryta under Subpart H may be withdrawn (which would also mean full approval would not be achieved, and could also mean that Oxbryta could be required to be removed from the market) if the required post-marketing confirmatory program is not completed or if the FDA determines the results do not verify clinical risk/benefit. We do not have a special protocol assessment agreement in place with the FDA for our HOPE-KIDS 2 Study.

We cannot be certain that Oxbryta, inclacumab or any other product candidates that we seek to develop will be successful in nonclinical studies or clinical trials or receive and maintain any regulatory approvals. If we do not receive regulatory approval for, regulatory approval is withdrawn from, or we otherwise fail to successfully commercialize Oxbryta, inclacumab or any other product candidates, we are likely to need to spend significant additional time and resources to identify other product candidates, advance them through nonclinical and clinical development and apply for regulatory approvals, which would adversely affect our business, prospects, financial condition and results of operations.

The development of Oxbryta as a potential disease-modifying anti-sickling agent in SCD patients represents a novel therapeutic approach, and there is a risk that the outcomes of our clinical trials will not be favorable or otherwise support any further decision to seek or grant or maintain any regulatory approval.

We have concentrated our product research and development efforts on developing novel, mechanism-based therapeutics for the treatment of grievous blood-based disorders with significant unmet need, and our future

success depends on the success of this therapeutic approach. The clinical trial requirements of the FDA and other comparable regulatory agencies and the criteria these regulators use to determine the safety and efficacy of any product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. To date, there are only four approved therapies for SCD, Oxbryta, crizanlizumab, hydroxyurea, and L-glutamine, and Oxbryta is the first approved therapy directed toward preventing the polymerization of hemoglobin molecules as a mechanism to reduce red blood cell sickling in SCD patients. As a result, the design and conduct of clinical trials for a therapeutic product candidate such as Oxbryta that targets this mechanism in SCD patients are subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of Oxbryta in SCD because of the limited clinical experience with its mechanism of action in these patients.

In particular, regulatory authorities in the United States and Europe have not issued definitive guidance as to how to measure and achieve efficacy in treatments for SCD. Based on our discussions with the FDA regarding the design for the HOPE Study, we determined to measure change in hemoglobin levels as the primary endpoint in the Phase 3 HOPE Study. This primary endpoint has not been used previously in a registration study for any SCD treatment. As a result, regulators outside of the United States have not determined that such data would signify a clinically meaningful result in SCD patients or would support seeking or obtaining regulatory approval.

We did not achieve statistically significant results with respect to either potential key secondary endpoint in Part A of the HOPE Study (relating to vaso-occlusive crisis episodes and to the PRO), and we may not achieve key endpoints in other clinical trials, such as any post-marketing confirmatory studies. In addition, we may not achieve the same results with respect to the primary endpoint in Part A of the HOPE Study in other ongoing of future clinical trials, including our ongoing TCD post-confirmatory study, the HOPE-KIDS 2 Study. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain and maintain regulatory approvals for Oxbryta, inclacumab and any other product candidates that we may pursue, would have an adverse impact on our business, prospects, financial condition and results of operations.

Results of earlier studies may not be predictive of future clinical trial results, and initial studies may not establish or maintain an adequate safety or efficacy profile for Oxbryta, inclacumab or other product candidates that we may pursue to justify proceeding to advanced clinical trials or an application for regulatory approval.

The results of nonclinical studies and clinical trials of Oxbryta, inclacumab and of any future product candidates that we may pursue may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial may not necessarily predict final results. For example, our nonclinical studies and clinical trials to date of Oxbryta in SCD have involved mostly one genotype of SCD, known as HbSS, and the results of these studies may not be replicated in other genotypes of SCD in clinical trials or in the general patient population. In addition, the results obtained in our development program for SCD patients aged 12 years and older, such as in our Phase 3 HOPE Study, may not be replicated in our ongoing studies in pediatric populations, including our HOPE-KIDS 1 Study and HOPE-KIDS 2 Study.

Products evaluated in post-marketing studies and product candidates in later stages of clinical trials may fail to demonstrate the desired safety and efficacy despite having progressed through nonclinical studies and earlier clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Since Oxbryta was approved under Subpart H requiring successful completion of a confirmatory clinical trial to obtain full FDA approval, if the results of our confirmatory study fail to demonstrate efficacy and safety adequate to obtain full regulatory approval for Oxbryta and maintain its marketing approval in the United States, this would have a substantial impact on our business, prospects, financial condition and results of operations.

In addition, nonclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval, in part because of differing interpretations of data and results by regulatory authorities. In addition, data and results from later studies or programs may conflict with earlier findings.

Our failure to demonstrate the required characteristics to support continued marketing of Oxbryta in the United States, full FDA approval, marketing approval for Oxbryta outside of the United States, or marketing approval for inclacumab or any other product candidate we may choose to develop, in any ongoing or future clinical trials would substantially harm our business, prospects, financial condition and results of operations.

Before we are able to obtain any marketing approval for Oxbryta outside of the United States, foreign regulatory authorities may impose additional requirements, the scope of which are not fully known at this time.

Before we can obtain any marketing approval for a drug candidate for any potential indication, we must successfully complete clinical trials. The FDA typically requires at least two pivotal, well-controlled Phase 3 clinical trials as a condition to the submission of an NDA and does not usually consider a single Phase 3 clinical trial to be adequate to support product approval. The FDA will typically only consider relying on one pivotal trial if, in addition, other well-controlled studies of the drug exist (for example, for other dosage forms or in other populations) or if the pivotal trial is a multi-center trial that provides highly reliable and statistically strong evidence of an important clinical benefit, such as effect on survival, organ function or PRO, and a confirmatory study would have been difficult to conduct on ethical grounds.

The FDA approved Oxbryta for the treatment of SCD under the accelerated approval pathway under Subpart H, and approval under this accelerated pathway means that we are required to conduct at least one post-marketing confirmatory study sufficient to verify Oxbryta's clinical benefit, which we intend to satisfy through our recently initiated HOPE-KIDS 2 Study. In Europe, we are in the process of seeking input from various European regulatory authorities regarding a pathway to approval of Oxbryta for the potential treatment of SCD patients based on the HOPE Study.

Foreign authorities may not consider the results of our ongoing, planned or potential future clinical trials of Oxbryta to be sufficient to maintain any approval outside of the United States. Any post-marketing confirmatory studies, if required, would result in increased costs and potential delays in the clinical development and marketing approval process outside the United States, which may require us to expend more resources than are available to us. In addition, it is possible that the FDA and the comparable foreign authorities may have divergent opinions on the elements necessary for a successful NDA and marketing authorization application, or MAA, respectively, which may cause us to alter our development, regulatory and/or commercialization strategies.

We may encounter substantial delays in conducting or completing our clinical trials, which in turn will result in additional costs and may ultimately prevent successful or timely completion of the clinical development and commercialization of Oxbryta, inclacumab or any other product candidates we may identify and pursue.

Before obtaining marketing approval from regulatory authorities for the sale of any our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. In addition, because the FDA approved Oxbryta under the accelerated approval pathway under Subpart H, we must conduct at least one post-marketing confirmatory study to verify clinical risk/benefit, which we intend to satisfy through our recently initiated HOPE-KIDS 2 Study. Clinical testing is expensive, time-consuming and uncertain as to outcome, and we cannot guarantee that any of our current or future clinical trials for Oxbryta or any other product candidates we may pursue will be conducted as planned or completed on

schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays or failures in reaching a consensus with regulatory agencies on study design, including clinical endpoints sufficient to support an approval decision;
- delays or failures to receive approval for conduct of clinical studies in one or more geographies, which could result in delays in enrollment and availability of data and results;
- delays or failures in reaching agreement on acceptable terms with a sufficient number of prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in obtaining required Institutional Review Board, or IRB, or ethics committee approval for each clinical trial site;
- delays in recruiting a sufficient number of suitable patients to participate in our clinical trials;
- imposition of a clinical hold by any regulatory authority, including if imposed due to safety concerns after an inspection of our clinical trial operations or study sites;
- failure by our CROs, clinical sites, participating clinicians or patients, other third parties or us to adhere to clinical trial, regulatory or legal requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCPs, or applicable regulatory requirements in other countries;
- delays in the testing, validation, manufacturing and delivery of sufficient quantities of Oxbryta or our product candidates or study related devices to the clinical sites and patients;
- delays in having patients enroll or complete participation in a study in accordance with applicable protocols or protocol amendments or return for post-treatment follow-up;
- reduction in the number of participating clinical trial sites or patients, including by dropping out of a trial;
- failure to address in an adequate or timely manner any patient safety concerns that arise during the course of a trial;
- unanticipated costs or increases in costs of clinical trials of Oxbryta or our product candidates;
- the occurrence of serious adverse events or other safety concerns associated with Oxbryta or our product candidates; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols or obtaining additional IRB or other approvals to conduct or complete clinical studies of Oxbryta or our product candidates.

We could also encounter delays if a clinical trial is suspended or terminated for any reason (which could occur as a result of termination by us, by the IRBs or ethics committees of the institutions in which such trials are being conducted, by an independent Safety Review Board for such trial, or by the FDA or other regulatory authorities). A clinical trial can be suspended or terminated for a wide variety of reasons, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by us, or the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, or failure to demonstrate a benefit from using Oxbryta or a drug candidate. In addition, if we make manufacturing or formulation changes to Oxbryta or our product candidates, we may need to conduct additional studies to bridge the development program from the data and results for the previous version to the modified version.

Clinical trial delays could shorten any periods during which we may have the exclusive right to commercialize a drug or product candidate or allow our competitors to bring products to market before we do,

which could impair our ability to successfully commercialize Oxbryta and our product candidates. In addition, any delays in completing our clinical trials will increase our costs, slow down our drug development and approval process or jeopardize our ability to maintain our current FDA approval of Oxbryta (or to achieve full FDA approval or any product approvals outside of the United States), and jeopardize our ability to continue or commence product sales and generate revenues. Any of these occurrences may significantly harm our business, prospects, financial condition and results of operations.

Difficulty in enrolling patients or maintaining compliance with dosing or other requirements in our clinical trials could delay or prevent clinical trials of Oxbryta or our product candidates, which in turn could delay or prevent our ability to obtain or maintain the regulatory approvals necessary to commercialize Oxbryta and our product candidates.

Identifying and qualifying patients to participate in our ongoing and planned clinical trials of Oxbryta, inclacumab, and any other product candidates that we may develop are critical to our success. Our clinical development efforts are initially focused on rare chronic blood diseases. For example, according to estimates by the Centers for Disease Control and Prevention, the prevalence of SCD, for which Oxbryta is indicated, is approximately 100,000 individuals in the United States. Accordingly, there are limited patient pools from which to draw for clinical trials in our target indications. We may not be able to identify, recruit, and enroll a sufficient number of subjects to complete our clinical trials of Oxbryta because of the perceived risks and benefits of Oxbryta, the availability of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective subjects and the subject referral practices of physicians, among other factors.

Further, if subjects in our clinical trials fail to comply with our dosing regimens or other requirements in our clinical trials, we may not be able to generate clinical data acceptable to the FDA or comparable regulatory authorities in our trials. For example, successful conduct of our HOPE-KIDS 2 Study (our post-approval confirmatory study) will require consistency in TCD measurements, which is why we are providing specific training and equipment to participating clinical trial sites in such clinical trial. Failure to achieve consistent high quality readings could result in data that are difficult to interpret or that delay or confound the results. If clinical sites or patients are unwilling or unable to participate in, complete or comply with the protocols for our studies for any reason, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of potential products may be delayed.

If we experience difficulties or delays in enrollment or are otherwise unable to successfully complete any clinical trial of Oxbryta, or any other product candidates we may pursue, our costs are likely to increase, and our ability to obtain and maintain regulatory approval (or achieve full regulatory approval of Oxbryta) and generate product revenue from Oxbryta and any of these product candidates will be impaired. Any of these occurrences would harm our business, prospects, financial condition and results of operations.

If serious adverse events or unacceptable side effects are identified during the development of Oxbryta or our product candidates, we may need to delay, limit or terminate our clinical development activities.

Clinical trials by their nature utilize only a small sample of the potential patient population. For example, our Phase 3 HOPE Study in SCD patients represents only a very small fraction of all patients with SCD. Side effects of Oxbryta, inclacumab or any other product candidates that we may develop may be uncovered only in later stages of clinical trials, or only in trials involving different patient populations (such as pediatric patients), or only during post-approval studies, such as our HOPE-KIDS 2 Study (our TCD confirmatory study), or the safety reporting required for approved products. Many approved drugs and product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented their further development. Moreover, a nonclinical toxicology study with Oxbryta in non-humans and clinical trials involving other hemoglobin modifiers (other than Oxbryta) have shown a decrease in oxygen delivery to tissue when a significant percentage of hemoglobin is modified. Hemoglobin modifiers, by increasing HbS’s affinity for oxygen, can cause a shift in oxygen levels, potentially resulting in tissue hypoxia. To date, clinical studies of

Oxbryta have not shown evidence of tissue hypoxia. However, if Oxbryta or any other product candidates that we may develop are associated with tissue hypoxia or any other undesirable side effects or unexpected undesirable characteristics in clinical trials or nonclinical studies, we may need to abandon their development or limit their development to more narrow uses or subpopulations, which could adversely affect our business, prospects, financial condition and results of operations. In addition, with respect to Oxbryta, such a result may also significantly impact or terminate our commercialization of Oxbryta.

Although the FDA and the European Commission have each granted orphan drug designation for Oxbryta for the potential treatment of SCD, we may not receive orphan drug designation for inclacumab or any other product candidates for which we may submit new applications for orphan drug designation, and any orphan drug designations that we have received or may receive in the future may not confer marketing exclusivity or other expected commercial benefits.

Our business strategy focuses on the development of product candidates for the treatment of rare, chronic blood disorders that may be eligible for FDA or European Union, or EU, orphan drug designation. Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. In the EU, the Committee for Orphan Medicinal Products of the EMA recommends orphan drug designation to promote the development of medical products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention, or treatment is authorized (or in other very limited circumstances). In 2015 and 2016, respectively, the FDA and the European Commission (acting on a positive recommendation by the EMA) each granted orphan drug designation for Oxbryta for the treatment of patients with SCD.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the United States and 10 years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Although the FDA and the EMA have each granted orphan drug designation to Oxbryta for the treatment of SCD, we may apply for orphan drug designation for Oxbryta in other jurisdictions or for other indications, or for inclacumab or other product candidates we may develop and pursue in the future. Applicable regulatory authorities may not grant us these additional designations. In addition, the exclusivity granted under any orphan drug designations that we have received from the FDA and the EMA, or may receive from any other regulatory authorities (if any), may not effectively protect Oxbryta or any other product candidate we pursue from competition because different drugs can be approved for the same condition. For example, in the United States, even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior, or the FDA can approve a competitor application for the same drug for a different indication than the orphan drug designation. In addition, legislators or regulators may elect to modify orphan drug exclusivity laws or regulations in ways that could materially impact existing or future orphan drug designations. Any inability to secure or maintain orphan drug designation or the exclusivity benefits of this designation would have an adverse impact on our ability to develop and commercialize our product candidates. In addition, even if any orphan drug designations we receive are maintained, we may be unable to realize significant commercial benefits from these regulatory exclusivities for Oxbryta or any other product candidate we pursue.

Risks Related to Our Reliance on Third Parties

We rely, and will continue to rely, on third parties to conduct some of our nonclinical studies and all of our clinical trials and also to perform other tasks for us. If these third parties perform in an unsatisfactory manner, it may harm our business.

We have relied upon and plan to continue to rely upon third-party CROs, including our CROs for our clinical trials of Oxbryta, to monitor and manage data for some of our ongoing nonclinical studies and for all of our clinical programs. We rely on these parties for execution of these nonclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials are conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with all applicable cGMPs, GCPs, and current good laboratory practices, or GLPs, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, manufacturing facilities, nonclinical testing facilities and other contractors. If we or any of our CROs or other vendors fail to comply with applicable regulations, the data generated in our nonclinical studies and clinical trials may be deemed unreliable and the applicable regulatory authorities may suspend regulatory approval or require us to repeat or to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the regulatory review and approval process, perhaps significantly.

In addition, the execution of nonclinical studies and clinical trials, the subsequent compilation and analysis of the data and results produced, and the supply of product for our trials and commercialization, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. These third parties may terminate their agreements with us upon short notice for our uncured material breach, or under certain other circumstances. If any of our relationships with our third-party CROs or other key vendors (including manufacturing and testing facilities) terminates, we may not be able to enter into arrangements with alternative CROs or other key vendors on a timely basis or at all, or do so on commercially reasonable terms. In addition, our CROs and other key vendors are not our employees, and except for remedies available to us under our agreements with them, we cannot control whether they devote sufficient time and resources to our programs. Furthermore, these third party CROs or other key vendors may also have relationships with other entities, some of which may be our competitors. If CROs or other key vendors do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data and results they obtain or the product they supply is compromised for any reason (including failure to adhere to our protocols, or regulatory requirements), our development activities may be extended, delayed, or terminated and we may not be able to seek, obtain or maintain regulatory approval for or successfully commercialize Oxbryta or any of our product candidates. Switching or adding CROs or any other key vendors involves additional cost, time and management resources and focus. In addition, our CROs or other key vendors may also generate higher costs than anticipated.

In addition, in connection with any NDA for our product candidates, pre-approval inspections by the FDA of our facilities and/or those of third parties involved in the drug development program may occur, including at clinical trial sites, CMOs or other third parties on which we are very reliant. Significant negative results from pre-approval inspections, if any, could materially delay potential approval of the drug candidate.

Accordingly, our dependence on third-party CROs and other key vendors may subject us to challenges, delays and costs that have a material adverse impact on our business, prospects, financial condition and results of operations.

We rely entirely on third parties for the manufacturing of Oxbryta, inclacumab and for any other product candidates we may pursue for nonclinical studies and clinical trials, and we expect to continue to do so for the commercialization of Oxbryta in the United States and for any other product commercialization we may conduct. Our business could be harmed if any of those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality or quantity levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture drug supplies for our ongoing commercialization of Oxbryta and for any clinical trials we are conducting or may conduct for Oxbryta, inclacumab or any other future product candidates, and we do not presently expect that we will establish or acquire the resources necessary to manufacture any of our product candidates on a commercial scale. We rely, and expect to continue to rely, wholly on third-party manufacturers to produce our product candidates for our clinical trials, as well as for commercial manufacture or any required post-marketing studies of Oxbryta, and we expect to do the same with respect to any other product candidates, if any, that receives marketing approval. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the trial, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay the clinical development and potential regulatory approval of our product candidates, which could harm our business and results of operations. We expect to rely on multiple third parties for the manufacture of commercial supplies of Oxbryta as well as for inclacumab or any other product candidates, if approved.

We may be unable to establish or maintain any agreements with third-party manufacturers for Oxbryta, inclacumab or any other product candidates, or to do so on acceptable terms. Even if we are able to establish or maintain agreements with third-party manufacturers for Oxbryta, inclacumab or any other product candidates, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach or termination of the manufacturing agreement by the third party or by us, including at a time that is costly or inconvenient for us;
- the inability of the third party to satisfy our ordering requirements as to quality, quantity and/or price, including, without limitation, potential impact on supply chain due to the impact of public health risks, such as the recent spread of the coronavirus;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the unwillingness of the third party to extend or renew terms with us when desired.

Our reliance on third-party manufacturers in connection with inclacumab entails additional potential risks, in connection with the transfer of technology from Roche to our third-party manufacturer for inclacumab, and the requirement for approval by the FDA of any Investigational New Drug application, or IND, from the new site, which may not be successful. In addition, because of our lack of experience manufacturing a biologic product, we will have greater reliance on the expertise and experience of our third-party manufacturer for inclacumab.

Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory and market risks for the production of such third-party materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may affect the regulatory assessment or clearance of our contract manufacturers' facilities generally, and industry consolidation, pricing or other market factors may cause our contract manufacturers to scale back, terminate or refuse to renew desired arrangements for our materials. If the FDA or a comparable foreign regulatory agency finds deficiencies in or does not approve these facilities for the manufacture of Oxbryta or our product candidates or if any agency later finds deficiencies or withdraws its approval in the future, we may need to find alternative manufacturing facilities. Any of these factors could negatively impact

our ability to commercialize Oxbryta or develop, obtain additional regulatory approval for or further market, as applicable, Oxbryta or our product candidates, if approved.

Oxbryta, inclacumab and any future product candidates that we may identify and pursue may compete with other product candidates and marketed drugs for access to manufacturing facilities. Any performance failure on the part of our existing or future manufacturers could delay or impair clinical development, marketing approval or commercialization. Although we believe we have adequate supplies to commercialize Oxbryta and conduct our ongoing clinical trials, if we are unable to enter into relationships with additional contract manufacturers, or our current or future contract manufacturers cannot perform as agreed, we may experience delays and incur additional costs in our continued commercialization and clinical development activities. Our current and anticipated future dependence upon others for the manufacturing of Oxbryta, our product candidates and any other marketed drugs may adversely affect our future profit margins and our ability to commercialize Oxbryta or any other product candidates that receive marketing approval on a timely and competitive basis.

If the contract manufacturing facilities on which we rely do not continue to meet regulatory requirements or are unable to meet our supply demands, our business will be harmed.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for Oxbryta, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMPs, or similar regulatory requirements outside the United States. These regulations govern manufacturing processes and procedures, including recordkeeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of Oxbryta or our product candidates. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, suspension of production, seizures or voluntary recalls of product candidates or marketed drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect clinical or commercial supplies of Oxbryta, inclacumab or any of our future product candidates.

Among other requirements, we or our contract manufacturers must supply all necessary documentation in support of an NDA or MAA seeking approval of a product candidate on a timely basis and must adhere to GLP and cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval for Oxbryta. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of Oxbryta, inclacumab or any of our future product candidates or the associated quality systems. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with these complex regulatory requirements. If these manufacturers, facilities, records or systems do not pass pre-approval inspections and reviews, additional regulatory approval of Oxbryta or regulatory approval of inclacumab or any of our other future product candidates may never be granted or may be substantially delayed.

In addition, at any time following approval of a product for sale, the regulatory authorities also may audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that could be costly or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through a supplement to an NDA, MAA variation or equivalent foreign regulatory filing, which could result in further delay, uncertainty and costs. Regulatory agencies may also require additional clinical studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our programs, results and activities (including commercial timelines).

These factors could cause us to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of Oxbryta or our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Our reliance on third parties requires us to share our trade secrets and confidential information, which increases the possibility that a competitor will discover them or that our critical information will be misappropriated or disclosed.

Because we rely on third parties to manufacture Oxbryta and to conduct other aspects of our clinical development activities, as well as for inclacumab and any other product candidates we may pursue, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, other forms of agreement with any collaborators, CROs, manufacturers and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets and confidential information may become known by our competitors, may inadvertently be incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or confidential information, or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

Our agreements typically restrict the ability of certain collaborators, CROs, manufacturers, other key vendors and consultants to publish data, although many of our contracts provide for the right to publish data in specified circumstances. A significant breach of these publication provisions could impair our competitive position. In addition, we conduct joint research and development programs that may require us to share trade secrets and other confidential information. Despite our efforts to protect our trade secrets and confidential information, our competitors may discover them, either through breach of agreements relating to these programs, independent development or publication of information where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets or confidential information would impair our competitive position and have an adverse impact on our business.

Risks Related to Our Intellectual Property

If we or our licensors are unable to obtain and maintain sufficient intellectual property protection for Oxbryta or our product candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize product candidates similar or identical to ours, and our ability to successfully commercialize Oxbryta, inclacumab and other product candidates that we may pursue may be impaired. Changes in patent policy and rules could impair our ability to protect our products and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

As is the case with other biopharmaceutical companies, our success depends in large part on our ability to obtain and maintain protection of the intellectual property, particularly patents, that we may exclusively license or own solely and jointly with others in the United States and other countries with respect to Oxbryta and our

product candidates and technology, including inclacumab. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to Oxbryta and our product candidates.

Obtaining and enforcing biopharmaceutical patents is costly, time consuming, uncertain and complex, and we or our licensors may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaboration partners fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors, licensees or collaboration partners are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. Further, we may not be aware of all third-party intellectual property rights potentially relating to Oxbryta or our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are and will remain highly uncertain. The patent examination process may require us or our licensors, licensees or collaboration partners to narrow the scope of the claims of our or our licensors', licensees' or collaboration partners' pending and future patent applications, which may limit the scope of patent protection that may be obtained. Our pending and future patent applications may not result in patents being issued that protect Oxbryta, inclacumab or any future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive product candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner, or by successfully seeking to narrow or invalidate our patents or render them unenforceable. Our and our licensors', licensees' or collaboration partners' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

We cannot assure you that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize Oxbryta or our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize Oxbryta, inclacumab or any future product candidates.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such

challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of Oxbryta or our product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

The United States has enacted and is currently implementing wide-ranging patent reform legislation. The United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would diminish the value of our patents and patent applications or narrow the scope of our patent protection, or weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first-to-file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or AIA, enacted in 2011, the United States has moved to a first-to-file system similar to other countries' systems. The AIA also includes a number of significant changes that affect the way patent applications are prosecuted, and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address certain of these provisions and the applicability of the AIA and new regulations remain to be issued. Accordingly, it is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of patents that may issue from such patent applications, all of which could have a material adverse effect on our business and financial condition. Any further changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and patent applications or narrow the scope of our potential patent protection.

We may become subject to claims alleging infringement of third parties' patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of Oxbryta, inclacumab or any future product candidates that we may develop.

We cannot assure that Oxbryta, inclacumab or any future product candidates that we may develop will not infringe existing or future third-party patents. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that we may infringe by commercializing Oxbryta or any future product candidates that we may develop. We may additionally be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of Oxbryta, inclacumab or any of our other product candidates.

We may in the future become party to, or be threatened with, adversarial proceedings or litigation against us regarding third party intellectual property rights with respect to Oxbryta, inclacumab or any other of our future product candidates, that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents. We may also be required to indemnify parties with whom we have contractual relationships against such claims. If a patent infringement suit were brought against us, we could be forced to

stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or to avoid potential claims, we may choose to seek, or be required to seek, a license from the third party to continue developing, manufacturing and marketing Oxbryta and our product candidates and would most likely be required to pay license fees or royalties or both, that could be significant. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property licensed to us. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. Even if we are successful in defending against such claims, such litigation can be expensive, uncertain, and time consuming to litigate, and would divert management's attention from our core business. Any of these events could harm our business significantly.

In addition to infringement claims against us, if third parties prepare and file patent applications in the United States that also claim technology similar or identical to ours, we may have to participate in interference or derivation proceedings in the USPTO to determine which party is entitled to a patent on the disputed invention. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights with respect to Oxbryta and our product candidates and technology.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors or other parties may infringe our patents or other intellectual property. Although we are not currently involved in any intellectual property litigation, if we were to initiate legal proceedings against a third party to enforce a patent covering Oxbryta or one of our product candidates, the defendant could counterclaim that the patent covering Oxbryta or our product candidate is invalid and/or unenforceable. In addition, there is an abbreviated regulatory pathway, under the Biologics Price Competition and Innovation Act of 2009, for the regulatory approval of biosimilar or interchangeable biologic products, which could create a litigation pathway for a third party to challenge patents covering inclacumab. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are multiple potential grounds for a validity challenge or an unenforceability assertion. The outcome following legal assertions of invalidity and unenforceability is often highly unpredictable.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms.

In addition, our defense of litigation, interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our business and operations including our ability to commercialize Oxbryta, raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring Oxbryta and our product candidates to domestic and foreign markets.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, inventorship disputes may arise from conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership or we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business and operations including our ability to raise the funds necessary to commercialize Oxbryta, continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We jointly own patents and patent applications with third parties. Our ability to exploit or enforce these patent rights, or to prevent the third party from granting licenses to others with respect to these patent rights, may be limited in some circumstances.

We jointly own certain patents and patent applications with third parties. In the absence of an agreement with each co-owner of jointly owned patent rights, we will be subject to default rules pertaining to joint ownership. Some countries require the consent of all joint owners to exploit, license or assign jointly owned patents, and if we are unable to obtain that consent from the joint owners, we may be unable to exploit the invention or to license or assign our rights under these patents and patent applications in those countries. For example, we have exclusively licensed from the Regents of the University of California, or Regents, worldwide patent rights covering Oxbryta and certain Oxbryta analogs, some of which patent rights we jointly own with the Regents. Additionally, in the United States, each co-owner may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third party infringement claims.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employees' former employers or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we are unable to protect the confidentiality of our trade secrets or other confidential information, the value of our technology could be materially adversely affected and our business would be harmed.

We seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and

collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Failure to obtain or maintain trade secrets or confidential know-how trade protection could adversely affect our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, our competitors could limit our use of our trade secrets or confidential know-how.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ outside firms and rely on them to pay many of these fees. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of complex procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, with a material adverse effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries worldwide, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection but patent enforcement is not strong. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights throughout the world. The legal systems of certain countries, particularly certain developing countries, do

not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the AIA has been recently enacted in the United States, resulting in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could, therefore, be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and provide opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

The USPTO recently has developed regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA, and, in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, the courts have yet to address many of these provisions and it is not clear what, if any, impact the AIA will have on the operation of our business. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors’ or collaboration partners’ patent applications and the enforcement or defense of our or our licensors’ or collaboration partners’ issued patents, all of which could have an adverse effect on our business and financial condition.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this has also contributed to uncertainty with respect to the value of patents, once obtained. Depending on decisions by the

U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. These changes could limit our ability to obtain new patents in the future that may be important for our business.

Risks Related to Our Business and Industry

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, commercial, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our team. Although we have employment offer letters with each of our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

Recruiting and retaining qualified scientific, medical, clinical, technical operations personnel and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize our product candidates. Competition to hire qualified personnel in our industry and geographic market is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We have recently implemented sales, marketing and distribution capabilities and expect to expand our product development capabilities, and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

With our recent establishment of infrastructure required for commercialization of Oxbryta and our current and planned product development activities, we have experienced significant and rapid growth in the number of our employees and the scope of our operations, particularly in the areas of sales, marketing and distribution, regulatory affairs, research and drug development. To manage this and future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations or recruit, train and retain a sufficient number of qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage our recent or future growth could delay the execution of our business plans or disrupt our operations.

If we are not successful in discovering, developing, acquiring or commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives could be impaired.

Although a substantial amount of our effort will focus on the continued commercialization, clinical testing and seeking of additional regulatory approval of Oxbryta, a key element of our strategy is to pursue, develop and commercialize a portfolio of products utilizing proprietary discovery and development technology. We are seeking to do so through our internal research programs and may also selectively pursue commercially synergistic in-licensing or acquisition of additional assets, such as inclacumab. With the exception of Oxbryta, all of our other potential product candidates remain in the earlier development stages. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may on further study be shown to have harmful side effects, lack of potential efficacy or other characteristics that indicate it is unlikely to meet applicable regulatory criteria or remain reasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If we fail to develop and successfully commercialize inclacumab or any other product candidates, our business and future prospects may be harmed and our business will be more vulnerable to any problems that we encounter in developing and commercializing Oxbryta.

If successful product liability claims are brought against us, we may incur substantial liability and costs. If the use of Oxbryta or our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to Oxbryta or our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.

The commercialization of Oxbryta, the use of Oxbryta and our product candidates, including inclacumab, in clinical trials and the sale of any other products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that Oxbryta or our product candidates may induce adverse events. The risk of product liability claims may be increased now that Oxbryta is approved and being sold in the United States. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;

- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- increased warnings on product labels or additional restrictions imposed by regulatory authorities;
- the recall of Oxbryta or our product candidates;
- the inability to commercialize Oxbryta or our product candidates; and
- decreased demand for Oxbryta or our product candidates, if approved for commercial sale.

We carry product liability insurance in amounts that we believe are sufficient in light of our current commercial activities and clinical programs, but we may not be able to obtain and maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

During the course of treatment, patients may suffer adverse events, including death, for reasons that may or may not be related to our products or product candidates. Such events can be time-consuming to address, could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, can delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products or product candidates, if approved, can require us to suspend or abandon our commercialization efforts of any approved product candidates, or can impair our ability to raise funds to pursue our development or commercialization efforts. Investigations of these events may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We may choose to use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on other programs or product candidates that may ultimately be more profitable or for which there is a greater likelihood of success.

Because we have limited resources, we may forego or delay the pursuit of opportunities with programs or product candidates or for indications that later prove to have greater commercial potential than those we do pursue. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates, including inclacumab, may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other partnering arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

Any collaboration arrangements that we might enter into in the future may not be successful, which could adversely affect our operations and financial condition.

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of Oxbryta, inclacumab and potential future product candidates. For example, in December 2019, we entered into the License and Collaboration Agreement with Syros Pharmaceuticals, Inc., to discover, develop and commercialize novel therapies for SCD and beta thalassemia. We may enter into additional collaboration arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies for our product candidates, both in the United States and internationally. To the extent that we decide to enter into collaboration agreements, we will face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for a product candidate, the costs and complexities of manufacturing and delivering a product candidate to patients, the potential of competing products, any uncertainty with respect to our ownership of technology, which can occur if there is a challenge to our ownership without regard to the merits of the challenge and industry and market conditions generally. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement, and we may not be successful in our efforts to establish and implement additional collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any collaboration that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of us and our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, costly and time-consuming disputes or termination of the collaboration arrangement. These disagreements can be difficult to resolve successfully, and any such termination or expiration would adversely affect us financially and could harm our business reputation. Many collaborations in the pharmaceutical and biotechnology industries do not result in successful outcomes, for a wide variety of reasons.

Our anticipated international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement and economic risks associated with doing business outside of the United States.

Our business strategy currently incorporates potential international expansion as we evaluate data from our Phase 3 HOPE Study, plan to conduct additional studies inside and outside the United States, and plan to seek to obtain regulatory approval to commercialize Oxbryta in additional patient populations inside the United States as well as in patient populations outside the United States. Doing business internationally involves a number of risks, including but not limited to:

- restrictions and obligations imposed by privacy regulations, such as provisions under the General Data Protection Regulation 2016/679, known as GDPR, applicable to the collection and use of personal health data in the European Union;
- multiple, conflicting, and changing laws and regulations such as tax laws, export and import restrictions, employment laws, regulatory requirements, and any requirements to obtain other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the sale or use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection for and enforcing our intellectual property;
- difficulties in staffing and managing our current and potential foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the FCPA, its books and records provisions, or its anti-bribery provisions.

Any such factors may impose additional responsibilities, obligations or liability in relation to our current and planned activities outside the United States, and we may be required to put in place additional mechanisms and make additional expenditures to ensure compliance with existing and new requirements, which could significantly harm our future international expansion and operations and, consequently, our results of operations.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations (collectively, "Trade Laws"). We can face serious consequences for violations.

Among other matters, these Trade Laws prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in

substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase over time. We engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our ability to invest in and expand our business and meet our financial obligations, to attract and retain third-party contractors and collaboration partners and to raise additional capital depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic and political conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, the results of presidential elections, other political influences and inflationary pressures. For example, an overall decrease in or loss of insurance coverage among individuals in the United States as a result of unemployment, underemployment or the potential repeal of certain provisions of the ACA, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, we may experience difficulties in the commercialization of Oxbryta and any eventual commercialization of our product candidates, and our business, results of operations, financial condition and cash flows could be adversely affected.

In addition, certain events have caused, and may cause or contribute to global financial crises, which have triggered and may in the future lead to extreme volatility and disruptions in the capital and credit markets. For example, in June 2016, the United Kingdom, or U.K., held a referendum in which voters supported the exit of the U. K. from the EU (known as “Brexit”), which could cause disruptions to and create uncertainty surrounding our business, including affecting our existing relationships with third parties that conduct some of our nonclinical studies and clinical trials and our ability to enter into new relationships with vendors and other third-party contractors, which could have an adverse effect on our business, financial results and operations. On January 31, 2020, the U.K. officially left the EU. Brexit has already and could continue to adversely affect European and/or worldwide economic and market conditions and could continue to contribute to instability in the global financial markets. The measures could also adversely affect our ability to raise additional capital, potentially disrupt the markets in which we currently conduct and plan to conduct operations and the tax jurisdictions in which we operate and adversely change tax benefits or liabilities in these or other jurisdictions. In addition, changes in, and legal uncertainty with regard to, national and international laws and regulations may present difficulties for our clinical and regulatory strategy.

A severe or prolonged economic downturn could result in a variety of risks to our business, including reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our relationships with our contractors and potential collaboration partners. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Misconduct or other improper activities of our employees, agents, contractors or collaborators could adversely affect our reputation and our business, prospects, operating results and financial conditions.

We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors or collaborators that would violate the law or regulations of the jurisdictions in which we operate, including FDA, healthcare, employment, foreign corrupt

practices, environmental, competition, and patient privacy regulations. Misconduct by our employees, agents, contractors, or collaborators could include intentional or unintentional failures to:

- comply with EMA or FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or EMA or comparable foreign regulatory authorities;
- comply with cGMP regulations and manufacturing standards that we have established and comply with applicable healthcare fraud and abuse regulations in the jurisdictions in which we operate;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

Additionally, our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and, therefore, involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA.

There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these requirements. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these requirements. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Our internal computer systems, or those of our third-party vendors, may fail or suffer security breaches, which could result in a material disruption of our business and operations.

Despite the implementation of security measures, our internal computer systems and those of our third-party vendors are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures, and the prevalent use of mobile devices that access confidential information increases the risk of data security breaches. With respect to our data and information technology infrastructure, we continue to invest in the protection of such infrastructure, but there can be no assurance that our efforts will prevent service interruptions or identify breaches in our systems.

If any such event were to occur and cause interruptions in our operations, it could adversely affect our business and operations or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. For example, the loss of data from completed or ongoing clinical trials or nonclinical studies for Oxbryta or any of our product candidates could harm our commercialization activities, result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches. As a result, any such cyber-attacks or breaches could have a material adverse effect on our business.

Risks Related to Our Equity Securities

The market price of our common stock has been and may continue to be highly volatile.

The market price of our common stock has experienced volatility since our initial public offering in August 2015 and is likely to continue to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- failure to successfully develop and commercialize Oxbryta, inclacumab or any other product candidates, including results relating to our launch and commercialization of Oxbryta in the United States;
- adverse results or delays in, or the halting of, our nonclinical studies or clinical trials, especially in our ongoing or future clinical program for Oxbryta for the treatment of SCD;
- reports of adverse events from our commercialization or clinical trials of Oxbryta, or from clinical trials of any other product candidates that we may develop;
- any delay in the review of, or potential action with respect to, our planned filing of an IND or NDA for inclacumab or for any other product candidates that we may develop and any adverse development or perceived adverse development with respect to the FDA's regulatory review of such filing;
- adverse regulatory decisions affecting Oxbryta, inclacumab or any other product candidates we may develop, including any delay in or denial of potential approval in accordance with our plans and expectations;
- inability to obtain additional funding;
- failure to prosecute, maintain or enforce our intellectual property rights;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- changes in laws or regulations applicable to Oxbryta or future products;
- inability to obtain adequate product supply for Oxbryta or our product candidates or the inability to do so at acceptable prices;

- introduction of new products, services or technologies by our competitors;
- failure to enter into or perform under strategic collaborations;
- failure to meet or exceed any financial projections that we or the investment community may provide;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock; and
- the other risks described in this “Risk Factors” section.

In addition, companies trading in the stock market in general, and the NASDAQ Stock Market, or NASDAQ, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. For example, negative publicity regarding drug pricing and price increases by pharmaceutical companies has negatively impacted, and may continue to negatively impact, the markets for biotechnology and pharmaceutical stocks. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management’s attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. Our operating results may fluctuate due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- our ability to commercialize Oxbryta or any of our product candidates, if approved, and the timing and costs of our commercialization activities;
- the timing and cost of, and level of investment in, research and development activities relating to Oxbryta and our product candidates, which may change from time to time;
- the timing and success or failure of clinical trials for Oxbryta and our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to obtain and maintain full regulatory approval for Oxbryta in the United States and to obtain regulatory approval of Oxbryta outside of the United States as well as regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;
- the cost of manufacturing Oxbryta and our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- our ability to attract, hire, train and retain qualified personnel;

- expenditures that we will or may incur to acquire or develop additional product candidates and technologies;
- the level of demand for Oxbryta and our product candidates, if approved, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies;
- the risk/benefit profile, cost and reimbursement policies with respect to Oxbryta and our products candidates, if approved, and existing and potential future drugs that compete with Oxbryta and our product candidates;
- whether Oxbryta or any of our product candidates are subject to any compliance-related challenges or sanctions, or any intellectual-property related challenges; and
- the changing and volatile U.S., European and global economic environments.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated financial guidance we may provide.

We incur significant costs, and expend significant time and effort, to comply with the rules applicable to us as a public company, including Section 404 of the Sarbanes-Oxley Act of 2002. If we fail to comply with these rules, including maintaining proper and effective systems of disclosure controls and internal controls over financial reporting, the accuracy and timeliness of our financial reporting may be adversely affected, and we could be subject to sanctions or other penalties that would harm our business.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or Exchange Act, Section 404, or Section 404, of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, and the rules and regulations of NASDAQ. The Exchange Act requires us to file accurate and timely quarterly, annual and current reports with the SEC. Section 404 generally requires our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting and requires us to include an opinion from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. We are also subject to significant corporate governance and executive compensation-related provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act, or Dodd-Frank, including the “say on pay” rules adopted by the SEC under Dodd-Frank. We incur significant legal, accounting and other expenses, and expend significant time and effort by management and other personnel, to comply with the rules applicable to us as a public company.

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our internal control over financial reporting for the purpose of providing the reports required by Section 404. Based on our assessment and using the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, criteria, our management, Chief Executive Officer and Chief Financial Officer, have concluded that, as of December 31, 2019, our internal control over financial reporting was effective. As required under Section 404 of Sarbanes-Oxley, our independent registered public accounting firm has tested the design and operating effectiveness of our controls over financial reporting and been required to provide an attestation report with respect to our internal control over financial reporting. During the course of our or their subsequent review and testing, however, material weaknesses or significant deficiencies may be identified and we may be unable to remediate them before we must provide the required reports. If material weaknesses or significant deficiencies in our internal control

over financial reporting are identified in the future, we may not detect or remediate errors on a timely basis and our consolidated financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from NASDAQ or other adverse consequences that would materially harm our business.

Moreover, stockholder activism, the current political environment, and increased levels of government scrutiny and regulatory reform may lead to substantial new regulations and disclosure obligations for public companies, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to any new compliance initiatives. In addition, any new rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage. New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of Sarbanes-Oxley and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, would result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

We are also authorized to grant stock options and other equity-based awards to our employees, directors and consultants pursuant to our Amended and Restated 2015 Stock Option and Incentive Plan, or 2015 Plan. The number of shares available for future grant under the 2015 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors or compensation committee to take action to reduce the size of the increase in any given year. In addition, in January 2017 our board of directors approved our 2017 Inducement Equity Plan and amended the plan in December 2019 with the Amended and Restated 2017 Inducement Plan, or the 2017 Inducement Plan. The 2017 Inducement Plan enables us and our subsidiaries to grant non-qualified stock options and other equity-based awards to induce employees who are not currently employed by us or our subsidiaries to accept employment with us or our subsidiaries. As of December 31, 2019, there were 837,550 shares reserved under the 2017 Inducement Plan (subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock) for issuance to new employees entering into employment with us. In addition, we have reserved shares of common stock for issuance pursuant to our 2015 Employee Stock Purchase Plan, or 2015 ESPP, which number of shares will automatically increase each year on January 1, from January 1, 2016 to January 1, 2025, by the lesser of (i) 3,000,000 shares of common stock, (ii) 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, or (iii) such lesser number of shares as determined by the administrator of our 2015 ESPP. Currently, we plan to register the increased number of shares available for issuance under the 2015 Plan and the 2015 ESPP each year. If our board of directors elects to increase the number of shares available for future grant under the 2015 Plan, the 2017 Inducement Plan or the 2015 ESPP, our stockholders may experience additional dilution, and our stock price may fall.

A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. A significant portion of our outstanding shares of common stock are held by a small number of stockholders, including our directors, officers and significant stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

We have also registered all shares of our common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. As a result, these shares will be available for sale in the public market subject to vesting arrangements and exercise of options, and restrictions under applicable securities laws. In addition, our directors, executive officers and certain affiliates have established or may in the future establish programmed selling plans under Rule 10b5-1 of the Exchange Act for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, five percent stockholders and their affiliates beneficially owned approximately 57.8% of our outstanding common stock as of February 1, 2020, based on the latest publicly available information.

These stockholders have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have broad discretion in the use of our capital resources consisting of cash and cash equivalents and short and long-term marketable securities, and may invest or spend our capital resources in ways with which you do not agree or in ways that ultimately may not increase the value of your investment.

We have broad discretion over the use of our capital resources consisting of cash and cash equivalents and short and long-term marketable securities. You may not agree with our decisions, and our use of our capital resources may not yield any returns to our stockholders. We expect to use our existing capital resources to continue the commercialization and clinical development of Oxbryta for the treatment of SCD, including in our recently completed Phase 3 HOPE Study, our ongoing Phase 2a HOPE-KIDS 1 Study, our recently initiated Phase 3 HOPE-KIDS 2 Study, our other research and development activities including other clinical and nonclinical studies, including for inclacumab, and for working capital and general corporate purposes. Our failure to apply our capital resources effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these resources. Our stockholders will not have the opportunity to influence our decisions on how to use our capital resources.

Provisions in our restated certificate of incorporation and amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Our restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our restated certificate of incorporation and amended and restated bylaws include provisions that:

- authorize “blank check” preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;

- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We experienced an ownership change as a result of our IPO and an ownership change as a result of our follow-on offerings, however we do not believe that these ownership changes will significantly limit our ability to use these pre-change NOL carryforwards. We may experience subsequent shifts in our stock ownership, including as a result of our future follow-on offering, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. In addition, pursuant to the Tax Cuts and Jobs Act of 2017, we may not use net operating loss carry-forwards arising in taxable years beginning after December 31, 2017 to reduce our taxable income in any year by more than 80% and we may not carry back any net operating losses arising in taxable years ending after December 31, 2017 to prior years. These new rules apply regardless of the occurrence of an “ownership change.”

We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock depends, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may not publish an adequate amount of research on our company, which may negatively impact the trading price for our stock. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline or increase in volatility. Further, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, in December 2017, Congress passed the Tax Cuts and Jobs Act, which made broad and complex changes to the tax laws. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders', tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

Our headquarters, where we have office and research and development laboratory space, is located in South San Francisco, California, where we lease 67,185 square feet of space pursuant to a noncancelable operating lease, or Lease.

In August 2018, we entered into an amendment to the Lease to relocate from the current headquarters to a to-be-constructed building consisting of approximately 164,150 rentable square feet of space when the building is ready for occupancy, or the Substitute Premise. The Substitute Premise is expected to be ready to occupy in the first half of 2020, at which time we will vacate the currently occupied facility and will have no further obligations with respect to the current facility.

We believe that our existing facilities and the Substitute Premise are sufficient for our current needs and for the foreseeable future.

Item 3. ***Legal Proceedings***

As of the date of this annual report on Form 10-K, we are not party to any material legal proceedings. In the future, we may become subject to legal proceedings and claims arising in the ordinary course of business.
Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse impact on our financial position, results of operations or cash flows. Regardless of the outcome, litigation can have an adverse effect on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. ***Mine Safety Disclosures***

Not applicable.

PART II

Item 5. *Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities*

Market Information

Our common stock began trading on The NASDAQ Global Select Market on August 12, 2015 and trades under the symbol "GBT". Prior to such time, there was no public market for our common stock.

Recent Sales of Unregistered Securities

During the year ended December 31, 2019, we did not issue or sell any unregistered securities not previously disclosed in a Quarterly Report on Form 10-Q or in a Current Report on Form 8-K.

Issuer Purchases of Equity Securities

We did not repurchase any securities during the quarter ended December 31, 2019.

Holders of Common Stock

As of February 21, 2020, there were 7 holders of record of 60,829,023 outstanding shares of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated by reference to Item 12 of Part III of this Annual Report.

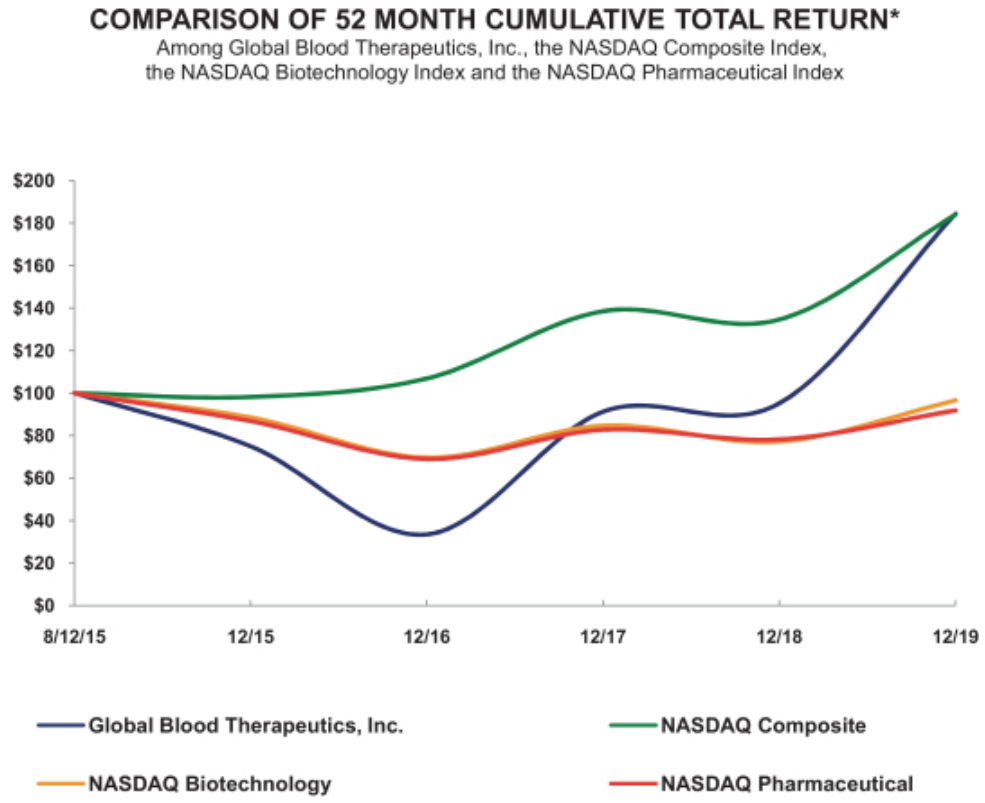
Dividend Policy

We have never declared or paid any cash dividends. We currently expect to retain all future earnings, if any, for use in the operation and expansion of our business, and therefore do not anticipate paying any cash dividends in the foreseeable future.

Performance Graph

The following is not deemed "filed" with the Securities and Exchange Commission and is not to be incorporated by reference into any filing we make under the Securities Act of 1933, as amended, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing.

The graph below matches Global Blood Therapeutics, Inc.'s cumulative 52-Month total shareholder return on common stock with the cumulative total returns of the NASDAQ Composite index, the NASDAQ Biotechnology index, and the NASDAQ Pharmaceutical index. The graph tracks the performance of a $100 investment in our common stock and in each index (with the reinvestment of all dividends) from August 12, 2015 to December 31, 2019.



*$100 invested on 8/12/15 in stock at the closing price on 8/12/15 or 7/31/15 in index, including reinvestment of dividends.
Fiscal year ending December 31.

	8/12/15	12/15	12/16	12/17	12/18	12/19
Global Blood Therapeutics, Inc.	**100.00**	**74.99**	**33.52**	**91.28**	**95.22**	**184.39**
NASDAQ Composite	**100.00**	**98.18**	**106.88**	**138.56**	**134.62**	**184.02**
NASDAQ Biotechnology	**100.00**	**88.59**	**69.68**	**84.75**	**77.24**	**96.64**
NASDAQ Pharmaceutical	**100.00**	**86.87**	**69.06**	**82.80**	**78.25**	**91.94**

The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Item 6. ***Selected Financial Data***

The information set forth below for the three years ended December 31, 2019 is not necessarily indicative of results of future operations, and should be read in conjunction with Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations and the Consolidated Financial Statements and related notes thereto included in Item 8 of this Annual Report on Form 10-K to fully understand factors that may affect the comparability of the information presented below (in thousands, except for share and per share data):

	Years Ended December 31,		
	2019	2018	2017
Summary of Operations Data:			
Product sales, net	$ 2,108	$ —	$ —
Costs and operating expenses			
Cost of sales	48	—	—
Research and development	174,556	131,307	87,807
Selling, general and administrative	117,088	51,435	31,438
Gain on lease modification[(1)]	(8,301)	—	—
Total costs and operating expenses	283,391	182,742	119,245
Loss from operations	(281,283)	(182,742)	(119,245)
Interest income, net	14,697	8,618	2,555
Other expenses, net	(180)	(69)	(334)
Net loss	$ (266,766)	$ (174,193)	$ (117,024)
Basic and diluted net loss per common share	$ (4.57)	$ (3.41)	$ (2.76)
Weighted-average number of shares used in computing basic and diluted net loss per common share	58,321,612	51,150,728	42,323,686

(1) During the year ended December 31, 2019, we recorded a gain on lease modification related to our existing premises located in South San Francisco, California.

(in thousands)	As of December 31,		
	2019	2018	2017
Selected Consolidated Balance Sheet Data:			
Cash and cash equivalents and marketable securities	$ 694,999	$ 591,815	$ 329,432
Working capital	556,544	452,007	298,048
Total assets	796,099	617,643	356,720
Long-term debt	73,559	—	—
Accumulated deficit	(738,916)	(472,150)	(297,957)
Total stockholders' equity	578,694	572,799	318,804

Item 7. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this annual report entitled "Selected Financial Data" and our consolidated financial statements and related notes included elsewhere in this annual report. This discussion and other parts of this annual report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions. In this annual report, words such as "may," "will," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements, as described elsewhere herein. As a result of many factors, including those factors set forth in the "Risk Factors" section of this annual report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. Founded in 2011, GBT is delivering on its goal to transform the treatment and care of sickle cell disease, or SCD, a lifelong, devastating inherited blood disorder that is marked by red blood cell, or RBC, destruction and occluded blood flow and hypoxia, leading to anemia, stroke, multi-organ failure, severe pain crises, and shortened patient life span. As a result of the historic lack of treatment options, patients with SCD suffer serious morbidity and premature mortality.

It is estimated the prevalence of SCD is approximately 100,000 individuals in the United States, where newborn screening is mandatory, and approximately 60,000 individuals in Europe. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually, and SCD is concentrated in populations of African, Middle Eastern and South Asian descent.

In late November 2019, we received U.S. Food and Drug Administration, or FDA, accelerated approval for our first medicine, Oxbryta (voxelotor) tablets for the treatment of SCD in adults and children 12 years of age and older. Oxbryta, an oral therapy taken once daily, is the first FDA-approved treatment that directly inhibits sickle hemoglobin polymerization, the root cause of SCD.

The accelerated approval of Oxbryta is based on clinically meaningful and statistically significant improvements in hemoglobin levels, accompanied by reductions in RBC destruction (hemolysis). Data from the Phase 3 HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS PolymErization) Study of 274 patients 12 years of age and older with SCD showed that, after 24 weeks of treatment, 51.1% of patients receiving Oxbryta achieved a greater than 1 g/dL increase in hemoglobin compared with 6.5% receiving placebo ($p<0.001$). The HOPE data also demonstrated corresponding improvements in other markers of hemolysis as well as a favorable safety and tolerability profile for Oxbryta.

In early December 2019, we began to make Oxbryta available to patients through our specialty pharmacy partner network. As part of this product launch, we are focused on securing reimbursement and expanding patient access. As part of our commitment to ensuring patient access, we established GBT Source Solutions, a comprehensive program for patients who are prescribed Oxbryta that provides a wide range of practical, educational and financial support customized to each patient's needs.

We are conducting and plan to conduct additional studies of Oxbryta, including our ongoing Phase 2a HOPE-KIDS 1 Study, an open-label, single- and multiple-dose Phase 2a study that is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD, and, as a condition of accelerated approval, our Phase 3 HOPE-KIDS 2 Study, a post-approval confirmatory study we initiated in December 2019 that is using transcranial Doppler, or TCD, flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. We also expect to conduct additional clinical studies of Oxbryta, including to seek to expand the potential approved product label into younger pediatric populations.

Beyond Oxbryta, we are also engaged in other research and development activities, all of which are currently in earlier development stages, including working on new targets to develop the next generation of treatments for SCD. As part of our efforts to build our pipeline, we regularly evaluate opportunities to in-license, acquire or invest in new business, technology or assets or engage in related discussions with other business entities.

In August 2018, we entered into the License Agreement, or Roche Agreement, with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and know-how to develop and commercialize inclacumab, a p-selectin inhibitor in development to address pain crises associated with the disease, including any modified compounds targeting p-selectin and derived from inclacumab, for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use. We are developing inclacumab as a treatment for VOCs in patients with SCD, and we expect to be able to leverage the safety data from Roche's prior clinical studies, which were not in patients with SCD, as we proceed with our development of inclacumab. We expect to initiate a pivotal clinical study in 2021.

In December 2019, we entered into the License and Collaboration Agreement, or Syros Agreement, with Syros Pharmaceuticals, Inc., or Syros, to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States. We will continue to seek the best scientific approaches to transform the treatment of these devastating lifelong diseases.

We own or jointly own and have exclusively licensed rights to Oxbryta and our product candidates in the United States, Europe and other major markets. We are the sole owner of issued U.S. patents covering Oxbryta, including its composition of matter, methods of use, formulations and polymorphs of Oxbryta. These issued U.S. patents covering Oxbryta will expire between 2032 and 2037, absent any applicable patent term extensions. We own or co-own additional pending patent applications in the United States and multiple foreign countries relating to Oxbryta.

Since our inception in 2011, we have devoted substantially all of our resources to identifying and developing Oxbryta and product candidates, including conducting clinical trials and nonclinical studies and providing general and administrative support for these operations.

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. We have financed our operations primarily through sale of equity securities and debt financing. In December 2018, we completed a follow-on offering and issued 3,409,090 shares of common stock at a price of $41.54 per share with proceeds of $141.1 million net of underwriting costs and commissions and offering expenses. In addition, in January 2019, we sold an additional 511,363 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $41.54 per share for proceeds of $21.2 million net of underwriting costs and commissions. In June 2019, we completed a follow-on offering and issued 3,375,527 shares of common stock at a price of $57.12 per share with proceeds of $192.4 million net of underwriting costs and commissions and offering expenses. In addition, in July 2019, we sold an additional 100,000 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $57.12 per share for proceeds of $5.7 million net of underwriting costs and commissions. In December 2019, we entered into a $150.0 million term loan agreement and drew down proceeds of $72.5 million net of debt issuance costs. We have an option to draw an additional $75.0 million until December 31, 2020.

Our net losses were $266.8 million for the year ended December 31, 2019, $174.2 million for the year ended December 31, 2018 and $117.0 million for the year ended December 31, 2017. As of December 31, 2019, we had an accumulated deficit of $738.9 million. Substantially all of our net losses have resulted from costs incurred in

connection with our research and development programs and from selling, general and administrative costs associated with our operations. We had $302.2 million in cash and cash equivalents and $392.8 million in marketable securities as of December 31, 2019.

Critical Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

Pursuant to Accounting Standards Codification, Topic 606, *Revenue from Contracts with Customers*, or ASC 606, we recognize revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration we expect to receive in exchange for those products or services.

To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect substantially all of the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

Product sales, net

Our product sales consist of U.S. sales of Oxbryta, which we began shipping to customers in December 2019. Prior to December 2019, we had no product sales. We sell Oxbryta to a limited number of specialty pharmacies and a specialty distributor, or collectively, Customers. These agreements with our Customers provide for transfer of title to the product at the time the product has been delivered to the Customers. The Customers subsequently dispense our product directly to a patient or resell our product to hospitals and certain pharmacies.

We recognize revenue on product sales when the Customers obtain control of our product, which occurs at a point in time, typically upon delivery to our Customers. It is at that point that we have a right to payment and that our Customers obtain title and the risks and rewards of ownership. Shipping and handling activities are considered to be fulfillment activities rather than a separate performance obligation. Payment terms are typically 30-60 days following delivery to our Customers. As allowed under ASC 606 via practical expedient, because payment is expected shortly after delivery, we do not adjust the amount of consideration expected to be received for the effects of a significant financing component.

We consider the effects of items that can decrease the transaction price such as variable consideration and consideration payable to Customers or payer. Amounts related to such items are estimated at contract inception and updated at the end of each reporting period as additional information becomes available. The amount of variable consideration may be constrained and is included in the transaction price only to the extent it is probable

that a significant reversal of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is resolved. Revenue from product sales is recorded after considering the impact of the following variable consideration amounts along with the constraint at the time of revenue recognition:

Rebates: We are subject to government mandated rebates for Medicaid Drug Rebate Program, Medicare Part D Prescription Drug Benefit Program, and other government health care programs in the United States. Rebate amounts are based upon contractual agreements or legal requirements with public sector benefit providers. We use the expected-value method for estimating these rebates based on statutory discount rates and expected utilization. The expected utilization of rebates is estimated based on third party market research data and data received from the specialty pharmacies and specialty distributor. Estimates for these rebates are adjusted quarterly to reflect the most recent information. We record an accrued liability for unpaid rebates related to products for which control has been transferred to Customers.

Prompt payment discounts: We provide discounts to our Customers if they pay for our products within a defined period of time after title transfers, which terms are explicitly stated in the contract. We use the most-likely-amount method for estimating prompt payment discounts. We expect that our Customers will earn prompt payment discounts. As a result, we deduct the full amount of those discounts from total product sales when revenues are recognized and record these discounts as a reduction of accounts receivable.

Co-payment assistance: We provide co-payment assistance to patients who have commercial insurance and meet certain eligibility requirements. We use the expected-value method for estimating co-payment assistance based on estimates of program redemption using data provided by third-party administrators. Estimates for the co-payment assistance are adjusted quarterly to reflect actual experience. We record an accrued liability for unredeemed co-payment assistance related to products for which control has been transferred to Customers.

Medicare Part D Coverage Gap: The Medicare Part D coverage gap is a federal program to subsidize the costs of prescription drugs for Medicare beneficiaries in the United States, which mandates manufacturers to fund a portion of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. Funding of the coverage gap is generally invoiced and paid in arrears. We estimate the impact of the Medicare Part D coverage gap using the expected-value method based on an amount expected to be incurred for the current quarter’s activity, plus an accrual balance for known prior quarters. Estimates for the impact of the Medicare Part D coverage gap are adjusted quarterly to reflect actual experience. We record an accrued liability for unpaid reserves related to the Medicare Part D coverage gap.

Product returns: Consistent with industry practice, we offer limited product return rights and generally allow for the return of product that is damaged or defective, or within a few months prior to and up to a few months after the product expiration date. We consider several factors in the estimation of potential product returns, including expiration dates of the product shipped, the limited product return rights, third-party data in monitoring channel inventory levels, shelf life of the product, prescription trends, and other relevant factors. We expect product returns to be immaterial. Other than these limited returns, we do not provide any product warranties.

Chargebacks: Chargebacks are discounts that occur when contracted parties purchase directly from a specialty distributor. Contracted parties, which currently consist primarily of Public Health Service Institutions and federal government entities purchasing via the Federal Supply Schedule, generally purchase the product at a discounted price. The specialty distributor, in turn, charge back the difference between the price initially paid by the specialty distributor and the discounted price paid to the specialty distributor by the contracted parties to us. The reserves for chargeback are based on known sales to contracted parties. We establish the reserves for chargebacks in the same period that the related revenue is recognized, resulting in a reduction of product revenue and receivables.

Distributor fees: Our specialty distributor provides distribution services to us for a fee, based on a contractually determined fixed percentage of sales. We estimate these distributor fees and record such estimates

in the same period the related revenue is recognized, resulting in a reduction of product revenue. We record an accrued liability for unpaid distributor fees.

Each of the above items is variable consideration, which we record at the time of revenue recognition, and require significant estimates, judgement and information obtained from external sources. If management's estimates differ from actuals, we will record adjustments that would affect product sales in the period of adjustment.

The following table summarizes activity with respect to our sales allowances and accruals for the year ended December 31, 2019 and 2018 (in thousands):

	Rebates, co-payment assistance, Medicare Part D coverage gap, product returns and distributor fees	Prompt payment discounts and chargebacks	Total
Balances at December 31, 2018	**$ —**	**$ —**	**$—**
Provision related to current period sales	529	113	642
Credit or payments made during the period	—	—	—
Balance at December 31, 2019	**$ 529**	**$ 113**	**$642**

Other revenue recognition considerations

Oxbryta is our only product. The only performance obligation included in our contracts is the delivery of Oxbryta to our Customers. Therefore, no allocation of transaction price amongst performance obligations is necessary. Consequently, the transaction price determined after considering the impacts of variable consideration is recognized at the time control is transferred to our Customers, which is upon delivery of Oxbryta to our Customers.

Because all sales of Oxbryta are in the United States and because our Customers are each a large distributor with similar variable consideration impacts, we provide revenue numbers on a total basis without further disaggregation. Additionally, we do not have any contract assets or liabilities, other than accounts receivable, related to our sales of Oxbryta.

Accruals of Research and Development and Manufacturing Costs

We record accruals for estimated costs of research, nonclinical and clinical studies and manufacturing development. These costs are a significant component of our research and development expenses. A substantial portion of our ongoing research and development activities are conducted by third-party service providers, including contract research organizations and contract manufacturing organizations. We also accrue for estimated costs of manufacturing activities for inventories. These costs are a significant component of the cost of our inventory.

We accrue the costs incurred under our agreements with these third parties based on actual work completed in accordance with agreements established with these third parties. We determine the accruals for research and development through discussions with internal personnel and external service providers as to the progress or stage of completion of the clinical studies and the agreed-upon fee to be paid for such services.

The accrual for contract manufacturing activities is based on an estimate of manufacturing activities completed to date, contractual rates, and amounts invoiced and paid to date at the end of each reporting period. We determine the percentage of manufacturing activities completed to date based on discussions with the contract manufacturing organization, oversight of the manufacturing activities and anticipated timeline.

As actual costs become known, we adjust our accruals. We have not experienced any material deviations between accrued costs and actual costs. However, actual clinical and manufacturing services performed, number of subjects enrolled, and the rate of subject enrollment may vary from our estimates, resulting in adjustments to research and development costs or inventories in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations or amounts of inventories capitalized.

Results of Operations

Comparison of the years ended December 31, 2019, 2018 and 2017

	Year Ended December 31,			Change 2019/2018		Change 2018/2017	
(in thousands, except percentages)	2019	2018	2017	$	%	$	%
Product sales, net	$ 2,108	$ —	$ —	$ 2,108	*	$ —	*
Costs and operating expenses:							
Cost of sales	48	—	—	48	*	—	*
Research and development	174,556	131,307	87,807	43,249	33%	43,500	50%
Selling, general and administrative	117,088	51,435	31,438	65,653	128	19,997	64
Gain on lease modification	(8,301)	—	—	(8,301)	*	—	*
Total costs and operating expenses	283,391	182,742	119,245	100,649	55	63,497	53
Loss from operations	(281,283)	(182,742)	(119,245)	(98,541)	54	(63,497)	53
Interest income, net	14,697	8,618	2,555	6,079	71	6,063	237
Other expenses, net	(180)	(69)	(334)	(111)	(161)	265	(79)
Net loss	$(266,766)	$(174,193)	$(117,024)	$ (92,573)	53%	$(57,169)	49%

* Change is not meaningful

Product sales, net

Product sales consist of sales of Oxbryta, which was approved by FDA in late November 2019. We commenced shipments of Oxbryta and fully launched with a deployed sales force in December 2019.

Cost of sales

Cost of sales of $48,000 for the year ended December 31, 2019, is related to certain costs incurred after FDA approval related to the cost of Oxbryta sold. Prior to receiving FDA approval for Oxbryta in November 2019, we recorded all costs incurred in the manufacture of Oxbryta as research and development expense. We expect to sell inventory previously expensed to research and development over approximately the current year, and accordingly we expect our costs of product sales of Oxbryta to increase as a percentage of net sales in future periods as we produce and sell inventory that reflects the full cost of manufacturing the product.

Research and development

Research and development expenses consist primarily of costs incurred for the development of Oxbryta and product candidates, which include:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- expenses incurred under agreements with consultants, third-party research and manufacturing organizations, and investigative clinical trial sites that conduct research and development activities on our behalf;

- the costs related to production of clinical supplies, including fees paid to contract manufacturers;
- laboratory and vendor expenses related to the execution of nonclinical studies and clinical trials;
- payments upon achievement of certain clinical development and regulatory milestones in relation with license agreement; and
- facilities and other allocated expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and clinical sites. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and the services are performed.

The largest component of our total operating expenses is our investment in research and development activities, including the clinical development of Oxbryta. We allocate research and development salaries, benefits, stock-based compensation and indirect costs to Oxbryta, inclacumab and other product candidates that we may pursue on a program-specific basis.

We expect our research and development expenses will increase in future periods as we continue to invest in research and development activities related to developing Oxbryta and product candidates, and as programs advance into later stages of development and we begin to conduct larger clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and research and development is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

The following table summarizes our research and development expenses incurred during the respective periods (in thousands, except percentages):

	Years Ended December 31,			Change 2019/2018		Change 2018/2017	
	2019	2018	2017	$	%	$	%
Costs incurred by development program:							
Oxbryta for the treatment of SCD	$117,827	$103,613	$64,860	$14,214	14%	$38,753	60%
Other preclinical programs	47,015	23,036	14,512	23,979	104	8,524	59
Inclacumab for the treatment of SCD	9,472	3,818	—	5,654	148	3,818	*
Oxbryta for the treatment of hypoxemic pulmonary disorders	242	840	8,435	(598)	(71)	(7,595)	(90)
Total research and development expenses	$174,556	$131,307	$87,807	$43,249	33%	$43,500	50%

* Change is not meaningful

Research and development expenses increased by $43.2 million, or 33%, to $174.6 million for the year ended December 31, 2019 from $131.3 million for the year ended December 31, 2018. The increase was primarily due to an increase of $14.2 million in internal and external costs related to our SCD program for Oxbryta as we advanced this program, including increased employee-related costs and increased costs associated with our New Drug Application, or NDA, submission activities. In addition, there was an increase of $5.7 million in internal and external costs associated with inclacumab driven by the pre-clinical research and manufacturing activities related to the Roche Agreement, which we entered into in August 2018. Furthermore, there was an

increase of $24.0 million in internal and external costs associated with preclinical programs, which is primarily driven by the $20 million upfront payment expensed under the Syros Agreement, which we entered into in December 2019. The increase is partially offset by a $0.6 million decrease in expenses related to our former hypoxemic pulmonary disorders program that was discontinued in October 2017. Stock-based compensation expense related to research and development was $19.1 million for the year ended December 31, 2019 and $12.7 million for the year ended December 31, 2018. The increase was primarily due to hiring additional personnel and stock price appreciation.

Research and development expenses increased by $43.5 million, or 50%, to $131.3 million for the year ended December 31, 2018 from $87.8 million for the year ended December 31, 2017. The increase was primarily due to an increase of $38.8 million in internal and external costs related to our SCD program for Oxbryta as we advanced this program, including expansion of our Phase 2a HOPE-KIDS 1 Study and our Phase 3 HOPE Study in 2018 as well as higher levels of manufacturing activities to support the program. In addition, there was an increase of $3.8 million in internal and external costs associated with inclacumab primarily driven by the upfront payment of $2.0 million under the Roche Agreement. Furthermore, there was an increase of $8.5 million in internal and external costs associated with preclinical programs. The increase is partially offset by a $7.6 million decrease in expenses related to our former hypoxemic pulmonary disorders program that was discontinued in October 2017. Stock-based compensation expense was $12.7 million for the year ended December 31, 2018 and $5.9 million for the year ended December 31, 2017. The increase was primarily due to hiring additional personnel, stock price appreciation and vesting of market-condition stock awards.

Selling, general and administrative expenses

Selling, general and administrative expenses consist primarily of costs incurred in our executive, commercial, finance, corporate development, human resource, information technology, legal, compliance and other general and administrative functions, which include:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- fees to third party vendors providing customer support services;
- expenses incurred under agreements with consultants; and
- facilities and other allocated expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

We expense all selling, general and administrative costs in the periods in which they are incurred. We expect our general and administrative expenses to continue to grow as we progress through the commercial launch of Oxbryta for the treatment of SCD.

General and administrative expenses increased by $65.7 million, or 128%, to $117.1 million for the year ended December 31, 2019 from $51.4 million for the year ended December 31, 2018. The increase was primarily due to an increase of $9.2 million in stock-based compensation expense, as a result of our hiring additional personnel and stock price appreciation, an increase of $24.6 million in salary and benefit costs due to a greater number of employees, an increase of $29.0 million in professional and consulting services due to the growth of our operations, such as commercial build-out during 2019, and an increase of $2.9 million in other general and administrative expenses due to the growth of our operations.

General and administrative expenses increased by $20.0 million, or 64%, to $51.4 million for the year ended December 31, 2018 from $31.4 million for the year ended December 31, 2017. The increase was primarily due to an increase of $9.6 million in stock-based compensation expense, as a result of our hiring additional personnel, stock price appreciation and vesting of market-condition restricted stock units, an increase of $4.9 million in salary and benefit costs due to higher headcounts, and an increase of $5.4 million in other general and administrative expenses, such as professional and consulting services, due to the growth of our operations.

Gain on lease modification

Gain on lease modification of $8.3 million for the year ended December 31, 2019 was related to our existing premises located in South San Francisco, California for 67,185 square feet of space in October 2019.

Interest income, net

Interest income, net was $14.7 million in 2019 compared to $8.6 million in 2018. The $6.1 million increase was due to the additional income earned from higher investment balances following our public equity offerings in 2019 and 2018, and our debt financing in 2019.

Interest income, net was $8.6 million in 2018 compared to $2.6 million in 2017. The $6.0 million increase was due to the additional income earned from higher investment balances following our public equity offerings in 2017 and 2018 as well as higher interest rates in 2018.

Income Taxes

As of December 31, 2019, we had federal net operating loss carryforwards of approximately $618.2 million to offset future federal taxable income, with $209.9 million available through 2037 and $408.3 million available indefinitely. We also had state net operating loss carryforwards of approximately $386.8 million that may offset future state taxable income, through 2039. Current federal and state tax laws include substantial restrictions on the utilization of net operating losses and tax credits in the event of an ownership change. Even if the carryforwards are available, they may be subject to annual limitations, lack of future taxable income, or future ownership changes that could result in the expiration of the carryforwards before they are utilized. At December 31, 2019, we recorded a 100% valuation allowance against our deferred tax assets of approximately $245.0 million, as at that time our management believed it was uncertain that they would be fully realized. If we determine in the future that we will be able to realize all or a portion of our net operating loss carryforwards, an adjustment to our net operating loss carryforwards would increase net income in the period in which we make such a determination.

Liquidity and Capital Resources

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. We have financed our operations primarily through sale of equity securities. In December 2018, we completed a follow-on offering and issued 3,409,090 shares of common stock at a price of $41.54 per share with proceeds of $141.1 million net of underwriting costs and commissions and offering expenses. In addition, in January 2019, we sold an additional 511,363 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $41.54 per share for proceeds of $21.2 million net of underwriting costs and commissions. In June 2019, we completed a follow-on offering and issued 3,375,527 shares of common stock at a price of $57.12 per share with proceeds of $192.4 million net of underwriting costs and commissions and offering expenses. In addition, in July 2019, we sold an additional 100,000 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $57.12 per share for proceeds of $5.7 million net of underwriting costs and commissions. In December 2019, we entered into a $150.0 million term loan agreement and drew down proceeds of $72.5 million net of debt issuance costs. As of December 31, 2019, we had $302.2 million in cash and cash equivalents and $392.8 million in marketable securities.

Our primary use of cash is to fund operations. Cash used to fund operations is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe that our existing capital resources will be sufficient to fund our planned operations for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could

utilize our available capital resources sooner than we currently expect. We believe we may continue to require additional financing to commercialize Oxbryta, advance Oxbryta through clinical development, advance inclacumab through clinical development, to develop other potential product candidates and to fund operations for the foreseeable future. We may continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. Our future funding requirements will depend on many factors, including:

- our ability to successfully commercialize Oxbryta, inclacumab and any other product candidates we may identify and develop in any territories;
- the manufacturing, selling, and marketing costs associated with the commercialization of Oxbryta and the potential commercialization of inclacumab and any other product candidates we may identify and develop, including the cost and timing of establishing or maintaining our sales and marketing capabilities in any territory(ies);
- the amount and timing of sales and other revenues from Oxbryta, inclacumab and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the time and cost necessary to wind down our completed Phase 3 HOPE Study, to conduct and complete multiple ongoing studies (including our HOPE-KIDS 1 Study, Phase 3 HOPE-KIDS 2 Study and our OLE study in HOPE study countries;
- the time and cost necessary to conduct and complete any additional clinical studies required to pursue additional regulatory approvals for Oxbryta for SCD, including our recently initiated Phase 3 HOPE-KIDS 2 Study (which is necessary to move from our current Subpart H approval to a full approval) and any studies to support potential label expansions into younger SCD pediatric populations, or any other post-marketing studies for Oxbryta for SCD;
- the progress, data and results of clinical trials of Oxbryta;
- the progress, timing, scope and costs of our nonclinical studies, our clinical trials and other related activities, including our ability to enroll subjects in a timely manner for our ongoing and future clinical trials of Oxbryta, inclacumab or any other product candidate that we may identify and develop;
- the costs of obtaining clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates we may identify and develop;
- our ability to advance our development programs, including for Oxbryta, inclacumab and any other potential product candidate programs we may identify and pursue, the timing and scope of these development activities, and the availability of approval for any of our other product candidates;
- our ability to successfully obtain any additional regulatory approvals from any regulatory authorities, and the scope of any such regulatory approvals, to market and sell Oxbryta, inclacumab and any other product candidates we may identify and develop in any territory(ies);
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies, and the costs and timing associated with any such acquisitions or in-licenses;
- our ability to attract, hire, and retain qualified personnel; and
- the costs of maintaining, expanding, and protecting our intellectual property portfolio.

Further, our operating plan may change, and we may need additional funds to meet operational needs and capital requirements for commercialization, clinical trials and other research and development expenditures. With

the exception of our Term Loan, we currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of Oxbryta and product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated commercialization, clinical trials and research and development activities.

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,		
(in thousands)	2019	2018	2017
Cash used in operating activities	$(194,417)	$(135,375)	$ (93,022)
Cash used in investing activities	(76,861)	(184,157)	(35,000)
Cash provided by financing activities	298,158	397,906	235,188
Net increase in cash, cash equivalents and restricted cash	$ 26,880	$ 78,374	$107,166

Cash flows from operating activities

Net cash used in operating activities was $194.4 million for the year ended December 31, 2019, consisting of a net loss of $266.8 million, which was partially offset by non-cash charges of $45.7 million for stock-based compensation, $8.3 million for gain on lease modification and $7.9 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $24.7 million of accrued liabilities primarily related to higher research and development activities and higher professional and consulting services due to the growth of our operations, an increase of $7.5 million of accrued compensation related to a higher number of employees, an increase of $4.5 million of accounts payable due to timing of payments, an increase of $2.6 million of accounts receivables as we commercially launched Oxbryta in December 2019, an increase of $3.1 million of prepaid expenses primarily due to advance payment made in connection with our inclacumab program and to support our commercialization of Oxbryta, and an increase of $1.3 million in inventories as we began capitalizing Oxbryta as inventory upon receipt of FDA approval in November 2019 and commercially launched Oxbryta in December 2019.

Net cash used in operating activities was $135.4 million for the year ended December 31, 2018, consisting of a net loss of $174.2 million, which was partially offset by non-cash charges of $30.1 million for stock-based compensation and $4.0 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $2.5 million of prepaid expenses due to advance payments made in connection with our Phase 3 HOPE Study and our Phase 2a HOPE-KIDS 1 Study, an increase of $8.0 million of accrued liabilities related to higher research and development activities and higher professional and consulting services due to the growth of our operations, an increase of $1.5 million of accrued compensation related to a higher headcount and a decrease of $1.3 million of accounts payable due to timing of payments. The remainder of changes in operating assets and liabilities are primarily related to continuous growth of our operations.

Net cash used in operating activities was $93.0 million for the year ended December 31, 2017, consisting of a net loss of $117.0 million, which was partially offset by non-cash charges of $13.7 million for stock-based compensation and $2.4 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $3.6 million of accrued compensation related to a higher headcount, an increase of $3.3 million of accrued liabilities along with an increase of $2.8 million of accounts payable related to an increase in our research and development activities and an increase in professional and consulting services due to the growth of our operations.

Cash flows from investing activities

Net cash used in investing activities for the year ended December 31, 2019 was $76.9 million, primarily consisting of the purchase of marketable securities of $434.9 million, and purchase of property and equipment for

our office and laboratory facility of $3.5 million, which are partially offset by maturities of marketable securities of $361.5 million.

Net cash used in investing activities for the year ended December 31, 2018 was $184.2 million, primarily consisting of the purchase of marketable securities of $361.4 million, and purchase of property and equipment for our office and laboratory facility of $4.8 million, which are partially offset by maturities of marketable securities of $182.0 million.

Net cash used in investing activities for the year ended December 31, 2017 was $35.0 million, primarily consisting of the purchase of marketable securities of $127.7 million, and purchase of property and equipment for our office and laboratory facility of $3.1 million, which are partially offset by maturities of marketable securities of $96.0 million.

Cash flows from financing activities

Cash provided by financing activities was $298.2 million for the year ended December 31, 2019. The cash provided by financing activities in 2019 was primarily from net proceeds of $219.4 million from the issuance of common stock in connection with our follow-on offerings completed in 2019, net proceeds of $72.5 million from the debt financing completed in 2019, and to a lesser extent, proceeds of $13.9 million from the issuance of common stock to participants in the ESPP and exercise of stock options, which are partially offset by $7.6 million of taxes paid related to net shares settlement of equity awards.

Cash provided by financing activities was $397.9 million for the year ended December 31, 2018. The cash provided by financing activities in 2018 was primarily from net proceeds of $396.5 million from the issuance of common stock in connection with our follow-on offerings completed in January 2018, March 2018 and December 2018, and to a lesser extent, proceeds of $7.7 million from the issuance of common stock to participants in the ESPP and exercise of stock options, which are partially offset by $6.3 million of taxes paid related to net shares settlement of equity awards.

Net cash provided by financing activities was $235.2 million for the year ended December 31, 2017. The cash provided by financing activities in 2017 was primarily from net proceeds of $232.0 million from the issuance of common stock in connection with our follow-on offerings completed during 2017 and to a lesser extent, proceeds of $3.9 million from the issuance of common stock to participants in the ESPP and exercise of stock options.

Off-Balance Sheet Arrangements

As of December 31, 2019, we had no off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the Securities and Exchange Commission, or SEC.

Contractual Obligations and Other Commitments

In December 2019, we entered into the Loan Agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent and a lender, and Biopharma Credit Investments V (Master) LP, as a lender, for a senior secured credit facility consisting of an initial term loan of $75.0 million, with an option to draw an additional $75.0 million until December 31, 2020. The first tranche of $75.0 million was funded in 2019. The Term Loan carries a 72-month term and provides for interest only payments for the first 39 months, followed by consecutive equal quarterly payments. The Term Loan bears interest at a floating per annum interest rate equal to 7.00% plus the greater of: (a) LIBOR rate or (b) 2%. Interest on amounts outstanding are payable quarterly in arrears. We are obligated to pay an additional fee to the Lenders determined by multiplying the principal amount being paid or prepaid multiplied by 2% when such payments are made. The obligations under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

In August 2018, we entered into an amendment to our Lease, or Lease Amendment, to relocate and expand our leased premises to a to-be-constructed-building consisting of approximately 164,150 rentable square feet of space, or Substitute Premises, when the Substitute Premises are ready for occupancy, or Substitute Premises Commencement Date. The Lease Amendment has a contractual term of 10 years from the Substitute Premises Commencement Date. The Lease Amendment grants us an option to extend the Lease Amendment for an additional 10-year period. We intend to vacate our current headquarters, or Existing Premises, and surrender and deliver the Existing Premises to the landlord on or before June 1, 2020, upon which time we will have no further obligations with respect to the Existing Premises.

The following table summarizes our contractual obligations under our loan agreement and the new and existing operating leases as of December 31, 2019 (in thousands):

		Payments Due by Period				
	Total	2020	2021	2022	2023	Thereafter
Term Loan	$ 107,718	$ 6,750	$ 6,750	$ 6,750	$ 31,406	$ 56,062
Operating lease obligations[1]	$ 131,884	$ 8,242	$ 11,736	$ 12,116	$ 12,508	$ 87,282
Total contractual obligations	$ 239,602	$ 14,992	$ 18,486	$ 18,866	$ 43,914	$ 143,344

(1) The table above is prepared under the assumption that the Substitute Premises Payment Commencement Date is April 1, 2020.

We have excluded from the above table $21.6 million in contractual obligations related to uncertain tax positions as we cannot make a reasonably reliable estimate of the period of cash settlement.

In December 2019, we entered into the Syros Agreement to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the agreement, subject to Syros' option to co-promote the first product in the United States. If we exercise the option, we will be responsible for all development, manufacture, regulatory activities and commercialization of the compound or product. Syros and we will be responsible for our own costs incurred to conduct research activities, except that we will fund up to $40.0 million in preclinical research for at least three years. Unless earlier terminated or extended, the research program under the agreement will end on the third anniversary of the agreement.

Under the terms of the Syros Agreement, we paid Syros an upfront payment of $20.0 million in January 2020, and, if we exercise our option under the agreement, we may be obligated to pay Syros up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the agreement. We will also be obligated to pay Syros, subject to certain reductions, tiered mid- to high-single digit royalties as percentages of calendar year net sales on any product resulting from the agreement.

In August 2018, we entered into the Roche Agreement pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and know-how to develop and commercialize inclacumab for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use. As of December 31, 2019, we have paid Roche an upfront payment of $2.0 million. We are obligated to make contingent payments to Roche totaling approximately $125.5 million in milestone payments for the SCD indication, including up to $40.5 million based on achievement of certain clinical development and regulatory milestones for inclacumab in the SCD indication, and up to $85.0 million based on achievement of certain thresholds for annual net sales of inclacumab. We are also obligated to make contingent payments to Roche up to an additional $5.5 million in milestone payments,

which are owed to a third party, based on achievement of such clinical development and regulatory milestones for inclacumab. We are also obligated to make contingent payments to Roche up to $19.25 million in milestone payments based on achievement of certain clinical development and regulatory milestones for inclacumab for any indication other than the SCD indication.

Recent Accounting Pronouncements

In August 2018, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40), Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, or ASU 2018-15. ASU No. 2018-15 requires a customer that is a party to a cloud computing service contract to follow the internal-use software guidance in Subtopic 350-40 to determine which implementation costs to capitalize and which costs to expense. The amendments in this update are effective for annual reporting periods beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption of the amendments in this update is permitted. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. We believe that the adoption of this new standard will have no material impact on our consolidated financial position or results of operations and have not elected to early adopt the amendment.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*. The new standard modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, including removals of, modification to, and additional disclosure requirements from Topic 820. The amendment of ASU No. 2018-13 removes disclosure requirements from Topic 820 in the areas of (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, (2) the policy for timing of transfers between levels, and (3) the valuation processes for Level 3 fair value measurements. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Except for certain amendments related to Level 3 fair value measurements, all the other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted upon issuance of ASU No. 2018-13. We believe that the adoption of this new standard will have no material impact on our consolidated financial position or results of operations and have not elected to early adopt the amendment.

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments (Topic 326)*, which amends the guidance on the impairment of financial instruments. The new standard adds to U.S. GAAP an impairment model that is based on expected losses rather than incurred losses, which is known as the current expected credit loss, or CECL model. The CECL model applies to most debt instruments (other than those measured at fair value), trade and other receivables, financial guarantee contracts, and loan commitments. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Early adoption of the amendments in this update is permitted. We believe that the adoption of this new standard will have no material impact on our consolidated financial position or results of operations and have not elected to early adopt the amendment.

Accounting Pronouncements Adopted

Leases (Topic 842)

In February 2016 the FASB issued ASU 2016-02, Leases (Topic 842 or ASU 2016-02). ASU 2016-02 amends several aspects of lease accounting, including requiring lessees to recognize almost all leases with a term greater than one year as a right-of-use, or ROU, asset and corresponding liability, measured at the present value of the lease payments. On January 1, 2019, we adopted Topic 842 using the modified retrospective approach as of the adoption date. Results for the three and nine months ended September 30, 2019 are presented under Topic 842. No prior period amounts were adjusted and continue to be reported in accordance with previous lease guidance, Accounting Standards Codification Topic 840, Leases, or Topic 840.

The new standard provides a number of optional practical expedients in transition. We elected the practical expedients to not reassess our prior conclusions about lease identification under the new standard, to not reassess lease classification, and to not reassess initial direct costs. We did not elect the practical expedient allowing the use of hindsight, which would require us to reassess the lease term of our leases based on all facts and circumstances through the effective date and did not elect the practical expedient pertaining to land easements as this is not applicable to our current contract portfolio.

The impact of our adoption of Topic 842 on the accompanying consolidated balance sheet as of January 1, 2019 was as follows (in thousands):

	December 31, 2018	Adjustments Due to our Adoption of Topic 842	January 1, 2019
Assets:			
Operating lease ROU assets	$ —	$ 14,177	$ 14,177
Liabilities:			
Operating lease liabilities, current as included in other liabilities, current	—	1,176	1,176
Deferred rent, current as included in other liabilities, current	712	(712)	—
Operating lease liabilities, noncurrent	—	24,754	24,754
Deferred rent, noncurrent as included in other liabilities, noncurrent	11,041	(11,041)	—

The adjustments due to our adoption of Topic 842 related to the recognition of ROU assets and lease liabilities for the existing operating leases. A cumulative-effect adjustment to beginning retained earnings was not required.

Other accounting pronouncements adopted

In February 2018, the FASB issued ASU No. 2018-02, *Income Statement—Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income*. The amendment of ASU No. 2018-02 states an entity may elect to reclassify the income tax effects of the Tax Cuts and Jobs Act of 2017 on items within accumulated other comprehensive income to retained earnings. The amendments in this update are effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2018. Early adoption is permitted. We adopted ASU No. 2018-02 in the first quarter of 2019. The adoption of this new standard did not have a material impact on our consolidated financial position or results of operations.

Item 7A. *Quantitative and Qualitative Disclosures about Market Risk*

Interest Rate Sensitivity

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We have invested primarily in money market funds, negotiable certificates of deposit, U.S. treasury notes, federal agency notes and corporate debt securities. The fair value of our investments, including those included in cash and cash equivalents and marketable securities, was $644.2 million as of December 31, 2019 and $591.7 million as of December 31, 2018.

Our investment policy is to limit credit exposure through diversification and investment in highly rated securities. We, along with our investment advisors, actively review current investment ratings, company specific events, and general economic conditions in managing our investments.

We performed a sensitivity analysis to determine the impact a change in interest rates would have on the value of our investment portfolio. Based on our investment positions as of December 31, 2019, a hypothetical 100 basis point increase in interest rate would result in a $1.9 million decline in the fair market value of our portfolio. Such losses would only be realized if we sold the investments prior to maturity.

We are also exposed to interest rate risk with respect to the senior secured credit facility that we entered into in December 2019, or Term Loan, that bears variable interest based on LIBOR. The outstanding principal balance of the Term Loan was $75.0 million as of December 31, 2019. We currently do not use interest rate derivative instruments to manage our exposure to interest rate fluctuations. We monitor our market interest rate risk exposures from the Term Loan using a sensitivity analysis. Our sensitivity analysis estimates the exposure to the Term Loan assuming a hypothetical 100 basis points change in interest rates on our $75.0 million of unhedged variable rate debt. A hypothetical 100 basis point change in interest rates would not result in material changes in the annual interest expenses recognized from the Term Loan.

These analyses do not consider the effect of any change in overall economic activity that could impact interest rates. Further, in the event of an increase in interest rates of significant magnitude, we may take actions to further mitigate our exposure to the change. However, due to the uncertainty of the specific actions that would be taken and their possible effects, these analyses assume no changes in our financial structure.

Item 8. ***Financial Statements and Supplementary Data***

GLOBAL BLOOD THERAPEUTICS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Years Ended December 31, 2019 and 2018

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Global Blood Therapeutics, Inc.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Global Blood Therapeutics, Inc. and subsidiary (the Company) as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2019, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019 based on criteria established in *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for leases as of January 1, 2019 due to the adoption of FASB Accounting Standards Update 2016-02, *Leases (Topic 842)*.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting in Item 9A. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an

understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgment. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Assessment of the estimated manufacturing activities completed to date

As discussed in Notes 2 and 5 to the consolidated financial statements, the Company has accrued manufacturing costs of $9,466 thousand as of December 31, 2019. This accrual is comprised of manufacturing activities conducted by third-party service providers, including contract manufacturing organizations. The accrual for contract manufacturing activities is based on an estimate of manufacturing activities completed to date, contractual rates, amounts invoiced and amounts paid at the end of each reporting period.

We identified the assessment of the estimated manufacturing activities completed to date as a critical audit matter. The percentage of manufacturing activities completed to date is a subjective estimate based on discussions with the contract manufacturing organizations, oversight of the manufacturing activities and the anticipated timeline. Testing of this estimate required a higher degree of auditor judgment to evaluate, and this estimate could have a significant impact on the amount of accrued manufacturing costs recorded by the Company.

The primary procedures we performed to address this critical audit matter included the following. We tested certain internal controls over the Company's accrued manufacturing cost process, including controls over the estimation of the percentage of manufacturing activities completed to date. We selected certain accrued manufacturing costs and assessed the Company's estimate of the manufacturing activities completed to date by:

(1) Inquiring with Company personnel responsible for overseeing the contract manufacturing activities to understand progress of the manufacturing activities; (2) Inspecting correspondence received from the contract manufacturing organizations and comparing the reported information to the Company's estimate; and (3) Inspecting executed change orders and original contract terms, including the timeline and budget, and comparing them to the Company's estimated manufacturing activities completed to date.

/s/ KPMG LLP

We have served as the Company's auditor since 2014.

San Francisco, California
February 26, 2020

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 302,237	$ 275,357
Short-term marketable securities	307,732	202,177
Accounts receivable, net	2,637	—
Inventories	1,277	—
Prepaid expenses	9,422	6,337
Other assets, current	4,692	1,909
Total current assets	627,997	485,780
Property and equipment, net	27,113	14,981
Long-term marketable securities	85,030	114,281
Operating lease right-of-use assets	52,775	—
Restricted cash	2,395	2,395
Other assets, noncurrent	789	206
Total assets	$ 796,099	$ 617,643
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 10,621	$ 6,046
Accrued liabilities	41,358	16,792
Accrued compensation	17,578	10,036
Other liabilities, current	1,896	899
Total current liabilities	71,453	33,773
Long-term debt	73,559	—
Operating lease liabilities, noncurrent	72,359	—
Other liabilities, noncurrent	34	11,071
Total liabilities	217,405	44,844
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 5,000,000 shares authorized at December 31, 2019 and 2018, respectively, and none issued and outstanding as of December 31, 2019 and 2018	—	—
Common stock, $0.001 par value, 150,000,000 shares authorized at December 31, 2019 and 2018, respectively; 60,644,380 and 55,640,299 shares issued and outstanding at December 31, 2019 and 2018, respectively	61	56
Additional paid-in capital	1,316,795	1,044,941
Accumulated other comprehensive income (loss)	754	(48)
Accumulated deficit	(738,916)	(472,150)
Total stockholders' equity	578,694	572,799
Total liabilities and stockholders' equity	$ 796,099	$ 617,643

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2019	2018	2017
Product sales, net	$ 2,108	$ —	$ —
Costs and operating expenses:			
Cost of sales	48	—	—
Research and development	174,556	131,307	87,807
Selling, general and administrative	117,088	51,435	31,438
Gain on lease modification	(8,301)	—	—
Total costs and operating expenses	283,391	182,742	119,245
Loss from operations	(281,283)	(182,742)	(119,245)
Interest income, net	14,697	8,618	2,555
Other expenses, net	(180)	(69)	(334)
Net loss	(266,766)	(174,193)	(117,024)
Other comprehensive loss:			
Net unrealized gain (loss) on marketable securities, net of tax	802	288	(170)
Comprehensive loss	$ (265,964)	$ (173,905)	$ (117,194)
Basic and diluted net loss per common share	$ (4.57)	$ (3.41)	$ (2.76)
Weighted-average number of shares used in computing basic and diluted net loss per common share	58,321,612	51,150,728	42,323, 686

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2016	36,638,156	$ 37	$ 367,371	$ (166)	$ (180,933)	$ 186,309
Issuance of common stock upon equity offerings, net of issuance costs	8,498,926	8	231,947	—	—	231,955
Issuance of common stock upon exercise of stock options	578,455	1	2,815	—	—	2,816
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	33,212	—	(238)	—	—	(238)
Issuance of common stock pursuant to ESPP purchases	76,585	—	1,050	—	—	1,050
Vesting of restricted stock purchases	306,389	—	424	—	—	424
Stock-based compensation expense	—	—	13,682	—	—	13,682
Net unrealized gain (loss) on marketable securities	—	—	—	(170)	—	(170)
Net loss	—	—	—	—	(117,024)	(117,024)
Balance at December 31, 2017	46,131,723	$ 46	$ 617,051	$ (336)	$ (297,957)	$ 318,804
Issuance of common stock upon equity offerings, net of issuance costs	8,403,826	8	396,026	—	—	396,034
Issuance of common stock upon exercise of stock options	596,434	1	6,021	—	—	6,022
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	255,039	1	(6,253)	—	—	(6,252)
Issuance of common stock pursuant to ESPP purchases	61,031	—	1,647	—	—	1,647
Vesting of restricted stock purchases	192,246	—	369	—	—	369
Stock-based compensation expense	—	—	30,080	—	—	30,080
Net unrealized gain (loss) on marketable securities	—	—	—	288	—	288
Net loss	—	—	—	—	(174,193)	(174,193)
Balance at December 31, 2018	55,640,299	$ 56	$1,044,941	$ (48)	$ (472,150)	$ 572,799
Issuance of common stock upon equity offerings, net of issuance costs	3,986,890	4	219,667	—	—	219,671
Issuance of common stock upon exercise of stock options	538,503	1	11,635	—	—	11,636
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	368,357	—	(7,617)	—	—	(7,617)
Issuance of common stock pursuant to ESPP purchases	63,280	—	2,361	—	—	2,361
Vesting of restricted stock purchases	47,051	—	157	—	—	157
Stock-based compensation expense	—	—	45,651	—	—	45,651
Net unrealized gain (loss) on marketable securities	—	—	—	802	—	802
Net loss	—	—	—	—	(266,766)	(266,766)
Balance at December 31, 2019	60,644,380	$ 61	$1,316,795	$ 754	$ (738,916)	$ 578,694

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2019	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$(266,766)	$(174,193)	$(117,024)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	8,605	4,607	1,658
Amortization (accretion) of premium (discount) on marketable securities	(2,057)	(661)	704
Non-cash interest expense	43	—	—
Amortization of operating lease right-of-use assets	1,327	—	—
Stock-based compensation	45,651	30,080	13,682
Gain on lease modification	(8,301)	—	—
Loss from disposal of fixed assets, net	—	45	—
Changes in operating assets and liabilities:			
Accounts receivables	(2,637)	—	—
Inventories	(1,277)	—	—
Prepaid expenses	(3,085)	(2,500)	(1,856)
Other assets, current	(2,112)	(1,278)	(162)
Accounts payable	4,499	(1,285)	2,771
Accrued liabilities	24,706	8,031	3,280
Accrued compensation	7,543	1,457	3,612
Other liabilities, current	(1,482)	742	(63)
Operating lease liabilities	893	—	—
Other liabilities, noncurrent	33	(420)	376
Net cash used in operating activities	(194,417)	(135,375)	(93,022)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(3,460)	(4,824)	(3,101)
Sale of property and equipment	45	75	—
Purchases of marketable securities	(434,919)	(361,405)	(127,724)
Maturities of marketable securities	361,473	181,997	96,000
Purchases of other assets	—	—	(175)
Net cash used in investing activities	(76,861)	(184,157)	(35,000)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock, net of issuance costs	219,443	396,501	231,955
Proceeds from issuance of long-term debt, net of debt issuance costs	72,475	—	—
Proceeds from issuance of common stock in settlement of employee stock purchase plan and exercise of stock options	13,857	7,669	3,892
Repurchases of unvested restricted stock purchases	—	(12)	(421)
Taxes paid related to net share settlement of equity awards	(7,617)	(6,252)	(238)
Net cash provided by financing activities	298,158	397,906	235,188
Net increase in cash, cash equivalents and restricted cash	26,880	78,374	107,166
Cash, cash equivalents and restricted cash at beginning of period	277,752	199,378	92,212
Cash, cash equivalents and restricted cash at end of period	$ 304,632	$ 277,752	$ 199,378
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:			
Accrued issuance costs	$ 85	$ 467	$ —
Leasehold improvements paid for by landlord	$ 17,231	$ —	$ 11,086
Accrued purchase of property and equipment	$ 78	$ 48	$ 1,536

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.
Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation

Global Blood Therapeutics Inc., or the Company, we, us, or our, was incorporated in Delaware in February 2011 and commenced operations in May 2012. We are a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. In late November 2019, we received U.S. Food and Drug Administration, or FDA, accelerated approval for our first medicine, Oxbryta® (voxelotor) tablets for the treatment of sickle cell disease, or SCD, in adults and children 12 years of age and older. In early December 2019, we began to make Oxbryta available to patients through our special pharmacy partner network. Our primary activities have been establishing our infrastructure, recruiting personnel, conducting development of Oxbryta and our product candidates, including establishing commercial operations, conducting clinical trials and raising capital. Our principal operations are based in South San Francisco, California, and we operate in one segment.

Follow-on Offerings

In December 2018, we completed a follow-on offering and issued 3,409,090 shares of common stock at a price of $41.54 per share with proceeds of $141.1 million net of underwriting costs and commissions and offering expenses. In addition, in January 2019, we sold an additional 511,363 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $41.54 per share for proceeds of $21.2 million net of underwriting costs and commissions.

In June 2019, we completed a follow-on offering and issued 3,375,527 shares of common stock at a price of $57.12 per share with proceeds of $192.4 million net of underwriting costs and commissions and offering expenses. In addition, in July 2019, we sold an additional 100,000 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $57.12 per share for proceeds of $5.7 million net of underwriting costs and commissions.

Need for Additional Capital

In the course of our development activities, we have sustained operating losses and we expect such losses to continue over the next several years. Our ultimate success depends on the outcome of our commercial launch of Oxbryta and research and development activities. Since inception through December 31, 2019, we have incurred cumulative net losses of $738.9 million. We expect to incur additional losses for the foreseeable future to commercialize Oxbryta and conduct product research and development, and expect to potentially raise additional capital to fully implement our business plan. If needed, we intend to raise such capital through borrowings, the issuance of additional equity, and potentially through strategic alliances with partner companies or other transactions. However, if such financing is not available at adequate levels, we will need to re-evaluate our operating plans. We believe that our existing cash and cash equivalents and marketable securities will be sufficient to fund our cash requirements for at least twelve months subsequent to the issuance of these financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America, or U.S. GAAP.

Use of Estimates

The preparation of the accompanying consolidated financial statements in accordance with U.S. GAAP requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the

disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of costs and expenses during the reporting period. We base our estimates and assumptions on historical experience when available and on various factors that we believe to be reasonable under the circumstances. We evaluate our estimates and assumptions on an ongoing basis. Our actual results could differ from these estimates under different assumptions or conditions.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. All significant intercompany transactions and balances have been eliminated upon consolidation.

Segment Reporting

We have determined that we operate in a single segment based upon the way the business is organized for making operating decisions and assessing performance. We have only one operating segment related to the development of pharmaceutical products. All property and equipment is maintained in the United States.

Cash and Cash Equivalents

We consider all highly liquid investments with original maturities of three months or less at the time of purchase to be cash equivalents. Cash equivalents, which consist primarily of amounts invested in money market accounts, are stated at fair value.

Investments in Marketable Securities

We invest in marketable securities, primarily money market funds, corporate debt securities, government securities, government agency securities, and certificates of deposits. We classify our marketable securities as available-for-sale securities and report them at fair value in cash equivalents or marketable securities on the consolidated balance sheets with related unrealized gains and losses included within accumulated other comprehensive income (loss) on the consolidated balance sheet. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income on the consolidated statements of operations and comprehensive loss. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in interest and other income (loss). The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

We regularly review all of our investments for other-than-temporary declines in estimated fair value. Our review includes the consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether we have the intent to sell the securities and whether it is more likely than not that we will be required to sell the securities before the recovery of their amortized cost basis. When we determine that the decline in estimated fair value of an investment is below the amortized cost basis and the decline is other-than-temporary, we reduce the carrying value of the security and record a loss for the amount of such decline.

Fair Value Measurement

The carrying amounts of certain financial instruments, including cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities.

Concentration of Risk

Credit Risk

We invest in a variety of financial instruments and, by our Board approved investment policy, limit the amount of credit exposure with any one issuer, industry or geographic area for investments other than instruments backed by the U.S. federal government.

Major Customers

We have entered into distribution agreements with certain limited specialty pharmacies and a specialty distributor. For the year ended December 31, 2019, our two largest customers represented approximately 90% of our product revenue.

Major Suppliers

We do not currently have any of our own manufacturing facilities, and therefore depend on an outsourced manufacturing strategy for the production of Oxbryta for commercial use and for the production of our product candidates for clinical trials. We have contracts in place with one third-party manufacturer that is approved for the commercial production of Oxbryta and one third-party supplier that is approved for Oxbryta's active pharmaceutical ingredient. Although there are potential sources of supply other than our existing manufacturers and suppliers, any new supplier would be required to qualify under applicable regulatory requirements.

Accounts Receivables, net

Accounts receivables are recorded net of estimates of variable consideration for which reserves are established and which result from discounts and chargebacks that are offered within contracts between us and a limited number of specialty pharmacies and a specialty distributor in the United States. These reserves are classified as reductions of accounts receivable.

We estimate the allowance for doubtful accounts based on an evaluation of aging of our receivables. Accounts receivable balances are written off against the allowance when it is probable that the receivable will not be collected. Given the nature and history of our accounts receivable, we determined that an allowance for doubtful accounts was not required at December 31, 2019.

Inventories

Inventories are stated at the lower of cost or estimated net realizable value, on a first-in, first out, or FIFO, basis. We use actual costs to determine our cost basis for inventories. Inventories consist of raw materials, work-in-process, and finished goods.

We began capitalizing costs as inventory when the product candidate received regulatory approval. Prior to regulatory approval, we recorded inventory costs related to product candidates as research and development expenses.

We periodically assess the recoverability of our inventory and reduce the carrying value of the inventory when items are determined to be obsolete, defective or in excess of forecasted sales requirements. Inventory write-downs for excess, defective and obsolete inventory are recorded as a cost of sales. There have been no write-downs of our inventories for the periods presented.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is provided using the straight-line method over the estimated useful lives of the assets, which is three years for

computer equipment and five years for laboratory equipment. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the improvements. Depreciation and amortization begins at the time the asset is placed in service. Maintenance and repairs are charged as expense in the statements of operations and comprehensive loss as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation and amortization are removed from the consolidated balance sheet and any resulting gain or loss is reflected in operations.

Impairment of Long-Lived Assets

We evaluate our long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows the asset is expected to generate over its remaining life. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. There have been no impairments of our long-lived assets for the periods presented.

Restricted Cash

Restricted cash consists of cash deposits held by our financial institution as collateral for our letter of credit under our facility lease.

Accruals of Research and Development and Manufacturing Costs

We record accruals for estimated costs of research, nonclinical and clinical studies and manufacturing development. These costs are a significant component of our research and development expenses. A substantial portion of our ongoing research and development activities are conducted by third-party service providers, including contract research organizations and contract manufacturing organizations. We also accrue for estimated costs of manufacturing activities for inventories. These costs are a significant component of the cost of our inventory.

We accrue the costs incurred under our agreements with these third parties based on actual work completed in accordance with agreements established with these third parties. We determine the accruals for research and development costs through discussions with internal personnel and external service providers as to the progress or stage of completion of the clinical studies and the agreed-upon fee to be paid for such services.

The accrual for contract manufacturing activities is based on an estimate of manufacturing activities completed to date, contractual rates, and amounts invoiced and paid to date at the end of each reporting period. We determine the percentage of manufacturing activities completed to date based on discussions with the contract manufacturing organization, oversight of the manufacturing activities and anticipated timeline.

As actual costs become known, we adjust our accruals. We have not experienced any material deviations between accrued costs and actual costs. However, actual clinical and manufacturing services performed, number of subjects enrolled, and the rate of subject enrollment may vary from our estimates, resulting in adjustments to research and development costs or inventories in future periods. Changes in these estimates that result in material changes to our accruals of research and development and manufacturing costs could materially affect our results of operations or amounts of inventories capitalized.

Revenue Recognition

Pursuant to Accounting Standards Codification, Topic 606, *Revenue from Contracts with Customers*, or ASC 606, we recognize revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration we expect to receive in exchange for those products or services.

To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect substantially all of the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

Product sales, net

Our product sales consist of U.S. sales of Oxbryta, which we began shipping to customers in December 2019. Prior to December 2019, we had no product sales. We sell Oxbryta to a limited number of specialty pharmacies and a specialty distributor, or collectively, Customers. These agreements with our Customers provide for transfer of title to the product at the time the product has been delivered to the Customers. The Customers subsequently dispense our products directly to a patient or resell our products to hospitals and certain pharmacies.

We recognize revenue on product sales when the Customers obtain control of our product, which occurs at a point in time, typically upon delivery to our Customers. It is at that point that we have a right to payment and that our Customers obtain title and the risks and rewards of ownership. Shipping and handling activities are considered to be fulfillment activities rather than a separate performance obligation. Payment terms are typically 30-60 days following delivery to our Customers. As allowed under ASC 606 via practical expedient, because payment is expected shortly after delivery, we do not adjust the amount of consideration expected to be received for the effects of a significant financing component.

We consider the effects of items that can decrease the transaction price, such as variable consideration and consideration payable to Customers or payer. Amounts related to such items are estimated at contract inception and updated at the end of each reporting period as additional information becomes available. The amount of variable consideration may be constrained and is included in the transaction price only to the extent it is probable that a significant reversal of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is resolved. Revenue from product sales is recorded after considering the impact of the following variable consideration amounts along with the constraint at the time of revenue recognition:

Rebates: We are subject to government mandated rebates for Medicaid Drug Rebate Program, Medicare Part D Prescription Drug Benefit Program, and other government health care programs in the United States. Rebate amounts are based upon contractual agreements or legal requirements with public sector benefit providers. We use the expected-value method for estimating these rebates based on statutory discount rates and expected utilization. The expected utilization of rebates is estimated based on third party market research data and data received from the specialty pharmacies and specialty distributor. Estimates for these rebates are adjusted quarterly to reflect the most recent information. We record an accrued liability for unpaid rebates related to products for which control has been transferred to Customers.

Prompt payment discounts: We provide discounts to our Customers if they pay for our products within a defined period of time after title transfers, which terms are explicitly stated in the contract. We use the most-likely-amount method for estimating prompt payment discounts. We expect that our Customers will earn prompt payment discounts. As a result, we deduct the full amount of those discounts from total product sales when revenues are recognized and record these discounts as a reduction of accounts receivable.

Co-payment assistance: We provide co-payment assistance to patients who have commercial insurance and meet certain eligibility requirements. We use the expected-value method for estimating co-payment assistance based on estimates of program redemption using data provided by third-party administrators. Estimates for the co-payment assistance are adjusted quarterly to reflect actual experience. We record an accrued liability for unredeemed co-payment assistance related to products for which control has been transferred to Customers.

Medicare Part D Coverage Gap: The Medicare Part D coverage gap is a federal program to subsidize the costs of prescription drugs for Medicare beneficiaries in the United States, which mandates manufacturers to fund a portion of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. Funding of the coverage gap is generally invoiced and paid in arrears. We estimate the impact of the Medicare Part D coverage gap using the expected-value method based on an amount expected to be incurred for the current quarter's activity, plus an accrual balance for known prior quarters. Estimates for the impact of the Medicare Part D coverage gap are adjusted quarterly to reflect actual experience. We record an accrued liability for unpaid reserves related to the Medicare Part D coverage gap.

Product returns: Consistent with industry practice, we offer limited product return rights and generally allow for the return of product that is damaged or defective, or within a few months prior to and up to a few months after the product expiration date. We consider several factors in the estimation of potential product returns, including expiration dates of the product shipped, the limited product return rights, third-party data in monitoring channel inventory levels, shelf life of the product, prescription trends, and other relevant factors. We expect product returns to be immaterial. Other than these limited returns, we do not provide any product warranties.

Chargebacks: Chargebacks are discounts that occur when contracted parties purchase directly from a specialty distributor. Contracted parties, which currently consist primarily of Public Health Service Institutions and federal government entities purchasing via the Federal Supply Schedule, generally purchase the product at a discounted price. The specialty distributor, in turn, charge back the difference between the price initially paid by the specialty distributor and the discounted price paid to the specialty distributor by the contracted parties to us. The reserves for chargeback are based on known sales to contracted parties. We establish the reserves for chargebacks in the same period that the related revenue is recognized, resulting in a reduction of product revenue and receivables.

Distributor fees: Our specialty distributor provides distribution services to us for a fee, based on a contractually determined fixed percentage of sales. We estimate these distributor fees and record such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue. We record an accrued liability for unpaid distributor fees.

Other revenue recognition considerations

Oxbryta is our only product. The only performance obligation included in our contracts is the delivery of Oxbryta to our Customers. Therefore, no allocation of transaction price amongst performance obligations is necessary. Consequently, the transaction price determined after considering the impacts of variable consideration is recognized at the time control is transferred to our Customers, which is upon delivery of Oxbryta to our Customers.

Because all sales of Oxbryta are in the United States and because our Customers are each a large distributor with similar variable consideration impacts, we provide revenue numbers on a total basis without further disaggregation. Additionally, we do not have any contract assets or liabilities, other than accounts receivable, related to our sales of Oxbryta.

Cost of Sales

Cost of sales consists primarily of direct and indirect costs related to the manufacturing of Oxbryta products sold, including third-party manufacturing costs, packaging services, freight, storage costs, allocation of overhead costs of employees involved with production, and Oxbryta net sales-based royalties payable to the Regents of the University of California. Costs incurred prior to FDA approval of Oxbryta in November 2019 have been recorded as research and development expense in our consolidated statement of operations.

Leases

Leases (Topic 842) Effective January 1, 2019

We determine if an arrangement is or contains a lease at inception by assessing whether the arrangement contains an identified asset and whether we have the right to control the identified asset. Right-of-use, or ROU, assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Lease liabilities are recognized at the lease commencement date based on the present value of future lease payments over the lease term. ROU assets are based on the measurement of the lease liability and also include any lease payments made prior to or on lease commencement and exclude lease incentives received and initial direct costs incurred, as applicable.

As most of our leases do not provide an implicit rate, we use our incremental borrowing rate based on the information available at the commencement date in determining the present value of future payments. We consider our credit risk, term of the lease, and total lease payments and adjust for the impact of collateral, as necessary, when calculating our incremental borrowing rates. The lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise any such options. Lease cost for our operating leases is recognized on a straight-line basis over the lease term.

We have elected to not separate lease and non-lease components for any leases within its existing classes of assets and, as a result, account for any lease and non-lease components as a single lease component. We have also elected to not recognize any leases within its existing classes of assets with a term of 12 months or less.

ROU assets and operating lease liabilities are remeasured upon certain modifications to leases using the present value of remaining lease payments and estimated incremental borrowing rate upon lease modification.

Leases (Topic 840) Prior to the Adoption of Topic 842

We enter into lease agreements for our office and laboratory facilities. These leases are classified as operating leases. Rent expense is recognized on a straight-line basis over the noncancelable term of the lease and, accordingly, we record the difference between cash rent payments and the recognition of rent expense as a deferred rent liability, which is included within other liabilities on the consolidated balance sheet. Incentives granted under our facilities leases, including rent holiday and allowances to fund leasehold improvements, are deferred and are recognized as adjustments to rental expense on a straight-line basis over the noncancelable term of the lease.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as a change in equity of a business enterprise during a period, resulting from transactions from non-owner sources. Our comprehensive income (loss) is comprised of net loss and changes in unrealized gains and losses on our marketable securities.

Research and Development

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to other nonemployees and entities that conduct certain research and development activities on our behalf. Amounts incurred in connection with license agreements are also included in research and development expense. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized and then expensed as the related goods are delivered or the services are performed.

Long-term Debt

Long-term debt consists of our loan agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent and a lender, and Biopharma Credit Investments V

(Master) LP, as a lender, and collectively, the Lenders. We accounted for the Term Loan as a debt financing arrangement. Interest expense is accrued using the effective interest rate method over the estimated period of the debt will be repaid. Debt issuance costs have been recorded as a debt discount in our consolidated balance sheets and are being amortized and recorded as interest expense throughout the life of the Term Loan using the effective interest rate method. We consider whether there are any embedded features in our debt instruments that require bifurcation and separate accounting as derivative financial instruments pursuant to Accounting Standards Codification, or ASC, Topic 815, *Derivatives and Hedging*.

Stock-Based Compensation

We measure and recognize stock-based compensation expense, including employee and non-employee equity awards, based on fair value at the grant date. We use the Black-Scholes-Merton option-pricing model to calculate fair value. Stock-based compensation expense recognized in the consolidated statements of operations is based on stock awards ultimately vested, taking into consideration actual forfeitures.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We must then assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to our lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

We recognize benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. It is our policy to include penalties and interest expense related to income taxes as a component of other expense and interest expense, respectively, as necessary. To date, there have been no interest or penalties incurred in relation to the unrecognized tax benefits.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding during the period, without consideration of common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given our net loss.

Recent Accounting Pronouncements

In August 2018, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40), Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, or ASU 2018-15. ASU No. 2018-15 requires a customer that is a party to a cloud computing service contract to follow the internal-use software guidance in Subtopic 350-40 to determine which implementation costs to capitalize and which costs to expense. The amendments in this update are effective for annual reporting periods beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption of the amendments in this update is permitted. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. We believe that the adoption of this new standard will have no material impact on our consolidated financial position or results of operations and have not elected to early adopt the amendment.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*. The new standard modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, including removals of, modification to, and additional disclosure requirements from Topic 820. The amendment of ASU No. 2018-13 removes disclosure requirements from Topic 820 in the areas of (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, (2) the policy for timing of transfers between levels, and (3) the valuation processes for Level 3 fair value measurements. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Except for certain amendments related to Level 3 fair value measurements, all the other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted upon issuance of ASU No. 2018-13. We believe that the adoption of this new standard will have no material impact on our consolidated financial position or results of operations and have not elected to early adopt the amendment.

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments (Topic 326)*, which amends the guidance on the impairment of financial instruments. The new standard adds to U.S. GAAP an impairment model that is based on expected losses rather than incurred losses, which is known as the current expected credit loss, or CECL model. The CECL model applies to most debt instruments (other than those measured at fair value), trade and other receivables, financial guarantee contracts, and loan commitments. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Early adoption of the amendments in this update is permitted. We believe that the adoption of this new standard will have no material impact on our consolidated financial position or results of operations and have not elected to early adopt the amendment.

Accounting Pronouncements Adopted

Leases (Topic 842)

In February 2016 the FASB issued ASU 2016-02, Leases (Topic 842 or ASU 2016-02). ASU 2016-02 amends several aspects of lease accounting, including requiring lessees to recognize almost all leases with a term greater than one year as a ROU asset and corresponding liability, measured at the present value of the lease payments. On January 1, 2019, we adopted Topic 842 using the modified retrospective approach as of the adoption date. Results for the three and nine months ended September 30, 2019 are presented under Topic 842. No prior period amounts were adjusted and continue to be reported in accordance with previous lease guidance, Accounting Standards Codification Topic 840, Leases, or Topic 840.

The new standard provides a number of optional practical expedients in transition. We elected the practical expedients to not reassess our prior conclusions about lease identification under the new standard, to not reassess lease classification, and to not reassess initial direct costs. We did not elect the practical expedient allowing the use of hindsight, which would require us to reassess the lease term of our leases based on all facts and circumstances through the effective date and did not elect the practical expedient pertaining to land easements as this is not applicable to our current contract portfolio.

The impact of our adoption of Topic 842 on the accompanying consolidated balance sheet as of January 1, 2019 was as follows (in thousands):

	December 31, 2018	Adjustments Due to our Adoption of Topic 842	January 1, 2019
Assets:			
Operating lease ROU assets	$ —	$ 14,177	$ 14,177
Liabilities:			
Operating lease liabilities, current as included in other liabilities, current	—	1,176	1,176
Deferred rent, current as included in other liabilities, current	712	(712)	—
Operating lease liabilities, noncurrent	—	24,754	24,754
Deferred rent, noncurrent as included in other liabilities, noncurrent	11,041	(11,041)	—

The adjustments due to our adoption of Topic 842 related to the recognition of ROU assets and lease liabilities for the existing operating leases. A cumulative-effect adjustment to beginning retained earnings was not required.

Other accounting pronouncements adopted

In February 2018, the FASB issued ASU No. 2018-02, *Income Statement—Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income*. The amendment of ASU No. 2018-02 states an entity may elect to reclassify the income tax effects of the Tax Cuts and Jobs Act of 2017, or Tax Cuts and Jobs Act, on items within accumulated other comprehensive income to retained earnings. The amendments in this update are effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2018. Early adoption is permitted. We adopted ASU No. 2018-02 in the first quarter of 2019. The adoption of this new standard did not have a material impact on our consolidated financial position or results of operations.

3. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). Our financial instruments consist of cash and cash equivalents, marketable securities, accounts receivables, accounts payable and accrued liabilities. Cash and cash equivalents and marketable securities reported at their respective fair values on our Consolidated Balance Sheets. The remaining financial instruments are reported on our Consolidated Balance Sheets at cost that approximate current fair values due to their relatively short maturities.

Assets and liabilities recorded at fair value on a recurring basis in the consolidated balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs

that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The following table summarizes our financial assets measured at fair value on a recurring basis (in thousands):

	December 31, 2019			
	Total	Level 1	Level 2	Level 3
Financial Assets:				
Money market funds	$250,535	$250,535	$ —	$ —
Corporate debt securities	152,149	—	152,149	—
U.S. government agency securities	95,032	—	95,032	—
Certificates of deposits	6,282	—	6,282	—
U.S. government securities	140,244	—	140,244	—
Total financial assets	$644,242	$250,535	$393,707	$ —

	December 31, 2018			
	Total	Level 1	Level 2	Level 3
Financial Assets:				
Money market funds	$275,234	$275,234	$ —	$ —
Corporate debt securities	110,027	—	110,027	—
U.S. government agency securities	88,028	—	88,028	—
Certificates of deposits	6,675	—	6,675	—
U.S. government securities	111,728	—	111,728	—
Total financial assets	$591,692	$275,234	$316,458	$ —

We estimate the fair values of our investments in corporate debt securities, government and government related securities and certificates of deposits by taking into consideration valuations obtained from third-party pricing services. The fair value of our marketable securities classified within Level 2 is based upon observable inputs that may include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. At December 31, 2019, the weighted average remaining contractual maturities of our Level 2 investments was less than one year and all of these investments are rated A-1/P-1/F1 or A/A2, or higher by Moody’s and S&P. There were no transfers between Level 1 and Level 2 during the periods presented.

4. Available-for-Sale Securities

Estimated fair values of available-for-sale securities are generally based on prices obtained from commercial pricing services. The following table is a summary of available-for-sale securities recorded in cash and cash equivalents, or marketable securities in our Consolidated Balance Sheets (in thousands):

	December 31, 2019				December 31, 2018			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
Financial Assets:								
Money market funds	$ 250,535	$ —	$ —	$ 250,535	$ 275,234	$ —	$ —	$ 275,234
Corporate debt securities	151,773	384	(8)	152,149	110,053	69	(95)	110,027
U.S. government agency securities	94,963	73	(4)	95,032	88,042	40	(54)	88,028
Certificates of deposits	6,239	43	—	6,282	6,681	1	(7)	6,675
U.S. government securities	139,978	266	—	140,244	111,730	60	(62)	111,728
Total	$ 643,488	$ 766	$ (12)	$ 644,242	$ 591,740	$ 170	$ (218)	$ 591,692

The following table summarizes the classification of the available-for-sale securities on our Consolidated Balance Sheets (in thousands):

	December 31, 2019	December 31, 2018
Cash and cash equivalents	$ 251,480	$ 275,234
Short-term marketable securities	307,732	202,177
Long-term marketable securities	85,030	114,281
Total	$ 644,242	$ 591,692

We do not intend to sell the investments that are in an unrealized loss position, and it is unlikely that we will be required to sell the investments before recovery of their amortized cost basis, which may be maturity. We have determined that the gross unrealized losses on our marketable securities at December 31, 2019 were temporary in nature. All unrealized losses from all marketable securities at December 31, 2019 are not material.

5. Balance Sheet Components

Property and Equipment

Property and equipment consist of the following (in thousands):

	December 31,	
	2019	2018
Laboratory equipment	$ 8,314	$ 7,363
Computer equipment	2,224	1,501
Leasehold improvements	13,785	13,785
Construction-in-progress	19,289	239
Total property and equipment	43,612	22,888
Less: accumulated depreciation and amortization	(16,499)	(7,907)
Property and equipment, net	$ 27,113	$14,981

Depreciation expense was $8.6 million for the year ended December 31, 2019, $4.7 million for the year ended December 31, 2018 and $1.7 million for the year ended December 31, 2017. Refer to Note 8—

Commitments and Contingencies for details on acceleration of depreciation expenses recognized during the year ended December 31, 2019.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2019	2018
Accrued research and development costs	$26,480	$ 4,150
Accrued manufacturing costs	9,466	10,971
Accrued professional and consulting services	4,564	1,016
Accrued sales deductions	529	—
Other	319	655
Total accrued liabilities	$41,358	$16,792

Other liabilities, current and noncurrent

Other liabilities consist of the following (in thousands):

	December 31,	
	2019	2018
Operating lease liabilities, current	$1,866	$ —
Restricted shares subject to repurchase, current	—	157
Deferred rent, current	—	712
Other payable, current	30	30
Total other liabilities, current	$1,896	$ 899
Deferred rent, noncurrent	$ —	$11,041
Other payable, noncurrent	34	30
Total other liabilities, noncurrent	$ 34	$11,071

6. Inventories

We began capitalizing inventories in November 2019 once the FDA approved Oxbryta. Inventories consist of the following (in thousands):

	December 31,	
	2019	2018
Raw materials	$ 700	$—
Work-in-process	525	—
Finished goods	52	—
Total inventories	$1,277	$—

7. Long-term Debt

Term Loan

On December 17, 2019, we entered into the Term Loan for a senior secured credit facility consisting of an initial tranche of $75.0 million and the option to draw an additional $75.0 million until December 31, 2020. The first tranche, in the amount of $75.0 million, was funded in connection with the closing date of the Term Loan in December 2019.

The Term Loan carries a 72-month term. The Term Loan bears interest at a floating per annum interest rate equal to 7.00% plus the greater of (a) the 3-month LIBOR rate and (b) 2%. In the event we default, the interest rate would be 3% above the rate that is otherwise applicable thereto. Interest on amounts outstanding are payable quarterly in arrears. The Term Loan repayment schedule provides for interest only payments for the first 39 months, followed by consecutive equal quarterly payments of principal and interest commencing in March 2023 and continuing through the maturity of December 2025.

We have the option to prepay all or a portion of the borrowed amounts under the Term Loan. If we exercise this option, we must pay a prepayment fee between 1% and 3% of the principal amount being prepaid depending on the timing of the prepayment, or Prepayment Fee. If the prepayment occurs before December 2022, we must also pay an amount equal to the sum of all interest that would have accrued and been payable from date of prepayment through December 2022, or Make Whole Amount. We are obligated to pay an additional fee to the Lenders determined by multiplying the principal amount being paid or prepaid multiplied by 2%, or Paydown Fee, when such payments are made.

In the event of default or change in control, all unpaid principal and all accrued and unpaid interest amounts (if any) become immediately due and payable, at which point, we will be subject to the Prepayment Fee, the Make Whole Amount (if any) and the Paydown Fee. Events of default include, but are not limited to, a payment default, a material adverse change, and insolvency. The obligations under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

Debt issuance costs paid directly to the Lenders of $1.1 million and the other debt issuance costs of $0.4 million were treated as discounts on the Term Loan. These debt discounts along with the Paydown Fee are being amortized or accreted to interest expenses throughout the life of the Term Loan using the effective interest rate method. As of December 31, 2019, there were unamortized issuance costs and debt discounts of $1.5 million, which were recorded as a direct deduction from the Term Loan on the consolidated balance sheet. In addition, we paid the Lenders $1.1 million for the option to draw the additional $75.0 million, which was capitalized as a deferred asset, which is included in other assets, current and amortized on a straight-line basis through December 31, 2020.

Future payments of principal and interest on the Term Loan as of December 31, 2019 (in thousands):

2020	$ 6,750
2021	6,750
2022	6,750
2023	31,406
2024	29,156
2025	26,906
Total minimum payments	107,718
Less amount representing interest	(31,218)
Less amount representing Paydown Fee	(1,500)
Long-term debt, gross	75,000
Discount on notes payable	(1,468)
Accretion of Paydown Fee	27
Long-term debt	$ 73,559

8. Commitments and Contingencies

Leases

We have operating leases for our headquarters, where we have office and research and development laboratory facilities, and equipment. Our leases have remaining lease terms of 1 to 10 years. Most of these leases

require monthly lease payments that may be subject to annual increases throughout the lease term. Certain of these leases include renewal options at our election, with renewal terms that can extend the lease term from 1 to 10 years. These optional periods have not been considered in the determination of the ROU assets or lease liabilities associated with these leases as we did not consider it reasonably certain that we would exercise the options.

For the year ended December 31, 2019, we incurred $7.8 million of lease costs included in operating expenses in the consolidated statement of operations in relation to these operating leases, of which $2.5 million was variable lease cost and not included within the measurement of our operating lease ROU assets and operating lease liabilities. The variable lease cost is comprised primarily of our cost in certain research and development arrangements that contain embedded equipment, and our proportionate share of operating expenses, property taxes, and insurance in relation with our facility lease. These costs are classified as operating lease expense due to our election to not separate lease and non-lease components.

Supplemental cash flow information related to leases for the period reported is as follows (in thousands, except weighted-average remaining lease term and weighted-average discount rate):

	Year Ended December 31, 2019
ROU assets obtained in exchange for new operating lease upon adoption of ASC 842	$ 14,177
Adjustment to ROU assets as a result of the lease modification for the Existing Premises	(13,802)
ROU assets obtained for new operating lease liabilities [(1)]	53,727
Cash paid for amounts included in the measurement of lease liabilities	4,481
Weighted-average remaining lease term of operating leases (in years)	10.1
Weighted-average discount rate of operating leases	8.66%

(1) Relates to ROU assets and operating lease liabilities for the Substitute Premises.

The majority of our lease costs are driven by our operating lease for our headquarters in South San Francisco, where we have office and research and development laboratory facilities.

In March 2017, we entered into a noncancelable operating lease, or Existing Lease, for approximately 67,185 square feet of space in South San Francisco, California, or Existing Premises. The date on which we became responsible for paying rent under the Existing Lease was December 15, 2017, or Rent Commencement Date. The Existing Lease expires 10 years after the Rent Commencement Date. The Existing Lease grants us an option to extend the Existing Lease for an additional 10-year period. Future minimum rental payments under the Existing Lease during the 10-year term are $48.5 million in the aggregate. The Existing Lease further provides that we are obligated to pay to the landlord certain costs, including taxes and operating expenses. The Existing Lease term commenced in November 2017 as we gained control over physical access to the Existing Premises. We have acquired $11.1 million of leasehold improvements at the Existing Premises with the tenant inducement allowance provided under the Existing Lease. We are required to repay $1.7 million of the tenant inducement allowance to the landlord in the form of additional monthly rent with interest applied over the term of the Existing Lease.

In August 2018, we entered into an amendment to the Existing Lease, or Lease Amendment, to relocate the leased premises from the Existing Premises to a to-be-constructed building consisting of approximately 164,150 rentable square feet of space, or Substitute Premises, when the Substitute Premises are ready for occupancy, or Substitute Premises Payment Commencement Date. The Lease Amendment has a contractual term, or Substitute Premises Term, of 10 years from the Substitute Premises Payment Commencement Date. The Lease Amendment grants us an option to extend the Lease Amendment for an additional 10-year period. Future minimum rental

payments under the Lease Amendment during the 10-year term are $121.5 million in the aggregate. Under the Lease Amendment, we are obligated to pay to the landlord certain costs, including taxes and operating expenses. The Lease Amendment also provides a tenant inducement allowance of up to $27.9 million, of which $4.1 million, if utilized, would be repaid to the landlord in the form of additional monthly rent with interest applied. As of December 31, 2019, we have capitalized $19.0 million of costs in construction-in-progress within property and equipment, net for construction of leasehold improvements at the Substitute Premises, which were mostly acquired with the tenant inducement provided under the Lease Amendment.

We intend to vacate the Existing Premises and surrender and deliver the Existing Premises to the landlord on or before June 1, 2020, upon which time we will have no further obligations with respect to the Existing Premises. Upon signing of the Lease Amendment, we re-evaluated the remaining useful life of the leasehold improvements at the Existing Premises and started to amortize the leasehold improvements over the remaining period of expected use, resulting in an acceleration of depreciation expenses for approximately $7.0 million during 2019.

On October 1, 2019, we determined that the Lease Amendment for the Substitute Premises had commenced as we had the right to control the Substitute Premises, which was deemed to be a lease modification. We determined the Lease Amendment consisted of two separate contracts under ASC 842. One contract was related to a new ROU asset for the Substitute Premises, which was to be accounted for as a new lease, and the other was related to the modification of the lease term of the Existing Premises.

With the commencement of the Lease Amendment, the lease term for the Existing Lease was reduced, with the modified lease term expiring on June 1, 2020. We determined that the reduction of the lease term would be accounted for as a lease modification to the Existing Lease. On October 1, 2019, we remeasured the present value of future lease payments during the modified lease term to be $2.9 million, using an incremental borrowing rate of approximately 8.78%. We recognized the amount of remeasurement of the lease liability as an adjustment to the ROU asset, reducing the carrying amount of the ROU asset to zero, and recognized a gain on lease modification of $8.3 million. As of December 31, 2019, the unamortized operating lease liability associated with the Existing Premises was $1.8 million.

On October 1, 2019, or Substitute Premises Commencement Date, we measured the present value of future lease payments that included the expected utilization of tenant inducements, using an incremental borrowing rate of approximately 8.66%. We recorded a ROU asset and a lease liability for $53.7 million associated with the Substitute Premises. During the year ended December 31, 2019, the landlord paid approximately $17.2 million out of tenant inducement allowances for construction of leasehold improvements at the Substitute Premises, which was recognized as an increase in the operating lease liability. As of December 31, 2019, the balances of the ROU asset and operating lease liability were approximately $52.8 million and $72.4 million, respectively.

As of December 31, 2019, the maturities of our operating lease liabilities under Topic 842 were as follows (in thousands):

Year ending December 31,	Amount
2020	(2,440)[(2)]
2021	11,736
2022	12,116
2023	12,508
2024	12,913
2025	13,333
Thereafter	61,035
Total lease payments	121,201
Less: Imputed interest	(46,976)
Present value of operating lease liabilities	$ 74,225

(2) Includes the expected receipt of the remaining tenant inducements of $10.7 million, which is partially offset by our lease payments of $8.3 million.

As of December 31, 2018, future annual minimum lease payments due under the Existing Lease and Lease Amendment under Topic 840 were as follows (in thousands):

Year ending December 31,	Amount[1]
2019	4,406
2020	6,513
2021	11,642
2022	12,020
Thereafter	102,776
Total	$ 137,357

(1) The table above is prepared under the assumption that the Substitute Premises Commencement Date is June 30, 2020.

Rent expense was $5.2 million for the year ended December 31, 2019, $3.6 million for the year ended December 31, 2018, and $2.0 million for the year ended December 31, 2017. The operating leases require us to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed above.

Indemnifications

We indemnify each of our directors and officers for certain events or occurrences, subject to certain limits, while the director is or was serving at our request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws. The term of the indemnification period lasts as long as a director may be subject to any proceeding arising out of acts or omissions of such director in such capacity. The maximum amount of potential future indemnification is unlimited; however, we currently hold director liability insurance. This insurance allows the transfer of risk associated with our exposure and may enable us to recover a portion of any future amounts paid. We believe that the fair value of these indemnification obligations is minimal. Accordingly, we have not recognized any liabilities relating to these obligations for any period presented.

Contingencies

In the ordinary course of business, we may be subject to legal claims and regulatory actions that could have a material adverse effect on our business or financial position. We assess our potential liability in such situations by analyzing potential outcomes, assuming various litigation, regulatory and settlement strategies. If we determine a loss is probable and its amount can be reasonably estimated, we accrue an amount equal to the estimated loss.

No losses and no provision for a loss contingency have been recorded to date.

Contingent Payments

In December 2019, we entered into an agreement, the Syros Agreement, with Syros Pharmaceuticals, Inc., or Syros, to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the agreement, subject to Syros' option to co-promote the first product in the United States. If we exercise the option, we will be responsible for

all development, manufacture, regulatory activities and commercialization of the compound or product. Syros and we will be responsible for our own costs incurred to conduct research activities, except that we will fund up to $40.0 million in preclinical research for at least three years. Unless earlier terminated or extended, the research program under the agreement will end on the third anniversary of the agreement.

Under the terms of the Syros Agreement, we paid Syros an upfront payment of $20.0 million in January 2020, and, if we exercise our option under the agreement, we may be obligated to pay Syros up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the agreement. We will also be obligated to pay Syros, subject to certain reductions, tiered mid- to high-single digit royalties as percentages of calendar year net sales on any product resulting from the agreement. As of December 31, 2019, we have recognized the $20.0 million upfront payment in our research and development costs for year ended December 31, 2019.

In August 2018, we entered into the License Agreement, or Roche Agreement, with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, “Roche”), pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and know-how to develop and commercialize inclacumab for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use. As of December 31, 2019, we have paid Roche an upfront payment of $2.0 million, which was recognized in our research and development costs for year ended December 31, 2018. We are obligated to make contingent payments to Roche totaling approximately $125.5 million in milestone payments for the SCD indication, including up to $40.5 million based on achievement of certain clinical development and regulatory milestones for inclacumab in the SCD indication, and up to $85.0 million based on achievement of certain thresholds for annual net sales of inclacumab. We are also obligated to make contingent payments to Roche up to an additional $5.5 million in milestone payments, which are owed to a third party, based on achievement of such clinical development and regulatory milestones for inclacumab. We are also obligated to make contingent payments to Roche up to $19.25 million in milestone payments based on achievement of certain clinical development and regulatory milestones for inclacumab for any indication other than the SCD indication.

9. Stockholders’ Equity

Common Stock Reserved for Issuance

We have reserved sufficient shares of common stock for issuance upon the exercise of stock options, vesting of restricted stock units and restricted shares subject to future vesting. Common stockholders are entitled to dividends if and when declared by the board of directors, subject to the prior rights of any preferred stockholders. As of December 31, 2019, no common stock dividends had been declared by the board of directors.

We have reserved shares of common stock for future issuance as follows:

	December 31,	
	2019	2018
Restricted shares subject to future vesting	—	47,051
Restricted stock units	1,848,772	975,419
Options issued and outstanding	3,573,860	3,243,551
Shares available for future grant under the 2015 Plan and 2017 Inducement Equity Plan	4,478,656	3,003,454
Employee stock purchase plan	252,655	240,935
Total	10,153,943	7,510,410

10. Share-based Compensation

Amended and Restated 2017 Inducement Equity Plan

In January 2017, we adopted the 2017 Inducement Equity Plan and amended the plan in December 2019 with the Amended and Restated 2017 Inducement Plan, or the 2017 Inducement Plan. Under the 2017 Inducement Plan, shares of our common stock are reserved for the issuance of non-qualified stock options and other equity-based awards to induce highly-qualified prospective officers and employees who are not currently employed by us or our subsidiaries to become employed with our company. Awards granted under the 2017 Inducement Plan expire no later than 10 years from the date of grant. For non-statutory stock options, the option price shall not be less than 100% of the fair market value on the day of grant. Options granted generally vest over four years and vest at a rate of 25% upon the first anniversary of the issuance date and $1/16^{th}$ per quarter over the following three years thereafter. Restricted stock units granted generally vest at a rate of 25% upon the first anniversary of the issuance date and $1/8^{th}$ per half year over the following three years thereafter. The number of shares initially reserved for grant is subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock. As of December 31, 2019, there were 837,550 shares reserved for the future issuance of equity awards under the 2017 Inducement Plan.

2015 Stock Option and Incentive Plan

In July 2015, we adopted the 2015 Stock Option and Incentive Plan, or 2015 Plan. Under the 2015 Plan, shares of our common stock are reserved for the issuance of stock options, restricted stock, and other equity-based awards to employees, non-employee directors, and consultants under terms and provisions established by the Board of Directors and approved by our stockholders at inception. Awards granted under the 2015 Plan expire no later than 10 years from the date of grant. For incentive stock options and non-statutory stock options, the option price shall not be less than 100% of the fair market value on the day of grant. If at the time we grant an option and the optionee directly or by attribution owns stock possessing more than 10% of the total combined voting power of all our classes of stock, the option price is required to be at least 110% of the fair market value on the day of grant. Options granted typically vest over a 4-year period but may be granted with different vesting terms. Restricted stock units granted generally vest at a rate of $1/8^{th}$ per half year over the 4-year period. As of December 31, 2019, there were 3,641,106 shares reserved for the future issuance of equity awards under the 2015 Plan.

2012 Stock Option and Grant Plan

In 2012, we adopted the 2012 Stock Option and Grant Plan, or 2012 Plan, under which our Board of Directors was authorized to grant incentive stock options to employees, including officers and members of the Board of Directors who are also employees of ours, and non-statutory stock options (options that do not qualify as incentive options) and/or our restricted stock and other equity-based awards to our employees, officers, directors, or consultants. Previously, we had initially reserved 2,785,713 shares of common stock for issuance under the 2012 Plan. On April 9, 2015 we increased the number of shares available under the 2012 Plan by 1,000,000 to a total of 3,785,713 shares. Awards granted under the 2012 Plan expire no later than 10 years from the date of grant. Upon adoption of the 2015 Plan, no new awards or grants are permitted under the 2012 Plan.

Stock Option Activity

The following table summarizes activity under our stock option plans, including the 2017 Inducement Plan, 2015 Plan and the 2012 Plan and related information (in thousands, except share and per share amounts and term):

	Number of Options	Weighted-Average Exercise Price	Weighted-Average remaining contractual term (years)	Aggregate Intrinsic Value
Outstanding—December 31, 2018	3,243,551	$ 29.74	7.96	
Options granted	1,026,965	50.04		
Options exercised	(538,502)	21.61		
Options canceled	(158,154)	42.26		
Outstanding—December 31, 2019	3,573,860	$ 36.24	7.55	$154,552
Vested and exercisable—December 31, 2019	1,884,402	$ 27.95	6.71	$ 97,114

The aggregate intrinsic value was calculated as the difference between the exercise price of the options and the fair value of our common stock as of December 31, 2019. The total intrinsic value of options exercised was $23.5 million for the year ended December 31, 2019, $23.4 million for the year ended December 31, 2018 and $11.3 million for the year ended December 31, 2017. The weighted-average estimated fair value of stock options granted was $32.30 for the year ended December 31, 2019, $33.58 for the year ended December 31, 2018 and $16.19 for the year ended December 31, 2017.

Stock Options Granted to Employees with Service-based Vesting Valuation Assumptions

The fair values of stock options granted to employees were calculated using the following assumptions:

	Year Ended December 31,		
	2019	2018	2017
Expected term (in years)	5.3-6.1	5.3-6.1	5.3-6.1
Volatility	69.8%-72.2%	68.7%-71.8%	68.9%-75.6%
Risk-free interest rate	1.4%-2.6%	2.6%-3.0%	1.8%-2.3%
Dividend yield	—	—	—

In determining the fair value of the options granted, we used the Black-Scholes-Merton option-pricing model and assumptions discussed below.

Expected Term—Our expected term represents the period that the options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). We have very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock option grants.

Expected Volatility—We use peer company price volatility as well as the historical volatility of our own common stock to estimate expected stock price volatility due to the limited trading history for our common stock since our IPO in August 2015. When selecting comparable publicly traded biopharmaceutical companies on which we have based our expected stock price volatility, we selected companies with comparable characteristics to us, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

Restricted Stock Units

In January 2017, the Compensation Committee of our Board of Directors approved the commencement of granting restricted stock units, or RSUs, to our employees. RSUs are share awards that entitle the holder to receive freely tradable shares of our common stock upon the completion of a specific period of continued service. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. RSUs granted are valued at the market price of our common stock on the date of grant. We recognize noncash compensation expense for the fair value of RSUs on a straight-line basis over the requisite service period of these awards.

The following table summarizes activity of RSUs granted to employees with service-based vesting under the 2017 Inducement Plan and 2015 Plan and related information (in thousands, except share, per share amounts and vesting period):

	Number of RSUs	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Vesting Period (years)	Aggregate Intrinsic Value
Non-vested units—December 31, 2018	816,169	$ 43.34	1.54	$ 33,504
RSUs granted	1,490,470	51.00		
RSUs vested	(331,046)	43.18		
RSUs forfeited	(126,821)	48.47		
Non-vested units—December 31, 2019	1,848,772	$ 49.19	1.54	$146,959

Restricted Stock Purchases

When Restricted Stock Purchases, or RSPs, are granted, the individual purchases the shares at the grant date fair value of the underlying common stock. The purchase of the stock is subject to forfeiture prior to vesting at the lower of fair value and the original purchase price. The award is treated similarly to an early exercise of stock options for accounting purposes.

A summary of our unvested restricted stock for the year ended December 31, 2019 is as follows:

	Number of RSPs	Weighted Average Grant Date Fair Value per Share
Outstanding—December 31, 2018	47,051	$ 2.24
RSPs vested	(47,051)	2.24
Outstanding—December 31, 2019	—	$ —

Market-Condition Awards Granted to Employees

On August 11, 2017, our Board of Directors approved awards up to an aggregate of 365,250 RSUs to certain of our senior management team under the 2015 Plan, the vesting of which was contingent upon a combination of

continued employment and achieving certain market capitalization milestones. The market-condition awards would not vest until the achievement of their respective market capitalization milestones, which must occur on or before December 31, 2019. The grant date fair value of these market-condition awards was estimated using a Monte Carlo simulation model. The derived service periods, which are the estimated periods of time that would be required to satisfy the market conditions, are also determined at the grant date. We record expense on a straight-line basis over the applicable derived service periods.

The following table summarizes activity of the market-condition awards under the 2015 Plan and related information (in thousands, except share, per share amounts and vesting period):

	Number of units	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Vesting Period (years)	Aggregate Intrinsic Value
Non-vested market-condition awards—December 31, 2018	159,250	$ 11.64	0.04	$ 6,537
Granted	—	—		
Vested	(156,000)	11.67		
Forfeited	(3,250)	10.49		
Non-vested market-condition awards—December 31, 2019	—	$ —	—	$ —

The following table summarizes the assumptions used to estimate the fair value of the market-condition awards during the year ended December 31, 2017:

Valuation date stock price	$28.55
Volatility	65.6%
Risk-free interest rate	1.4%
Dividend yield	—

We recognized $36,500, $3.1 million and $2.2 million in stock-based compensation expense related to the market-condition awards for the year ended December 31, 2019, December 31, 2018 and December 31, 2017 respectively.

Employee Stock Purchase Plan

In July 2015, we adopted the 2015 Employee Stock Purchase Plan, or 2015 ESPP. Under the 2015 ESPP, our employees may purchase common stock through payroll deductions at a price equal to 85% of the lower of the fair market value of the stock at the beginning of the offering period or at the end of each applicable purchase period. The 2015 ESPP provided for offering periods of six months in duration. As approved by the Compensation Committee of the Board of Directors in December 2017, the 2015 ESPP provides for offering periods of two years in duration with purchase periods occurring every six months during an offering period. The purchase periods end on either January 31 or July 31. Contributions under the 2015 ESPP are limited to a maximum of 15% of an employee's eligible compensation. ESPP purchases are settled with common stock from the ESPP's previously authorized and available pool of shares. During the year ended December 31, 2019, 63,280 shares were issued under the ESPP for $2.4 million.

The fair values of the rights granted under the 2015 ESPP were calculated using the following assumptions:

	Year Ended December 31, 2019	Year Ended December 31, 2018
Expected term (in years)	0.5 – 2.0	0.5 – 2.0
Volatility	46.5-75.4%	59.2-65.4%
Risk-free interest rate	1.7-2.6%	1.6-2.7%
Dividend yield	— %	— %

Stock-Based Compensation Expense

Total stock-based compensation recognized by functions was as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Research and development	$19,140	$12,747	$ 5,905
General and administrative	26,511	17,333	7,777
Total stock-based compensation expense	$45,651	$30,080	$13,682

Unrecognized Stock-Based Compensation Expense and Weighted-Average Remaining Amortization Period

As of December 31, 2019, the unrecognized stock-based compensation cost, and the estimated weighted-average amortization period, using the straight-line attribution method, was as follows (in thousands, except amortization period):

	Unrecognized Compensation Cost	Weighted-average remaining amortization period (years)
Options	$ 45,430	0.9
Restricted stock units	78,914	1.8
ESPP	1,387	—
Total unrecognized stock-based compensation expense	$ 125,731	2.7

11. Defined Contribution Plan

In 2013, we began to sponsor a 401(k) retirement plan, in which substantially all of our full-time employees are eligible to participate. Eligible participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. We made contributions to the Plan for eligible participants, and recorded contribution expenses of $1.4 million for the year ended December 31, 2019, $0.8 million for the year ended December 31, 2018 and $0.3 million for the year ended December 31, 2017.

12. Income Taxes

In December 2017, the President signed the Tax Cuts and Jobs Act, or Tax Act. The Tax Act, among other things, lowered the U.S. corporate income tax rate from 35% to 21% effective January 1, 2018. Consequently, our gross deferred tax assets as of December 31, 2017 were significantly reduced to reflect the estimated impact of the Tax Act. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The significant reduction in our gross deferred tax assets are fully offset by a reduction in valuation allowance, resulting in no impact to our income tax expense.

The components of the loss before income taxes were as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Loss before provision for income taxes:			
United States	$(266,595)	$(174,190)	$(101,288)
International	(167)	—	(15,736)
	$(266,762)	$(174,190)	$(117,024)

No provision for income taxes was recorded for the years ended December 31, 2019, December 31, 2018 and December 31, 2017. We have incurred net operating losses for all the periods presented. We have not reflected any benefit of such net operating loss (NOL) carryforwards in the accompanying consolidated financial statements. We have established a full valuation allowance against the related deferred tax assets due to the uncertainty surrounding the realization of such assets.

The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2019	2018	2017
Federal statutory income tax rate	21.0%	21.0%	34.0%
State taxes	9.7	1.3	—
Federal and state tax credits	4.9	7.1	7.3
Change in valuation allowance	(37.2)	(33.3)	(14.8)
Foreign rate differential	—	1.7	(4.6)
Officer compensation limitation	(1.0)	(0.7)	(0.9)
Stock based compensation/Non-deductible changes in fair value	1.7	2.9	0.7
Liquidation of foreign entities	0.9	—	—
Tax reform—tax rate change	—	—	(21.7)
Provision for Taxes	0.0%	0.0%	0.0%

The components of the deferred tax assets and liabilities are as follows (in thousands):

	December 31, 2019	December 31, 2018
Deferred tax assets:		
Net operating loss carryforwards	$ 157,685	$ 90,861
Tax credits	62,862	47,374
Operating lease liability	16,177	2,471
Accruals and reserves	3,996	1,954
Stock based compensation	11,166	4,838
Intangibles	8,243	—
Other	408	—
Gross deferred tax assets	260,537	147,498
Valuation allowance	(245,000)	(145,788)
Net deferred tax assets	15,537	1,710
Operating lease – ROU asset	(14,971)	—
Property and equipment	(352)	(1,710)
Other	(214)	—
Gross deferred tax liabilities	(15,537)	(1,710)
Net deferred tax assets	$ —	$ —

Realization of the deferred tax assets is dependent upon future taxable income, if any, the amount and timing of which are uncertain. We have established a valuation allowance to offset deferred tax assets as of December 31, 2019 and 2018 due to the uncertainty of realizing future tax benefits from our net operating loss carryforwards and other deferred tax assets. The valuation allowance increased approximately $99.2 million, $57.9 million, and $17.8 million during the years ended December 31, 2019, 2018, and 2017, respectively. The increase in the valuation allowance is mainly related to the increase in net operating loss carryforwards and the increase in tax credits generated during the respective taxable years.

As of December 31, 2019, we had federal net operating loss carryforwards of approximately $618.2 million to offset future federal taxable income, with $209.9 million available through 2037 and $408.3 million available indefinitely. We also had state net operating loss carryforwards of approximately $386.8 million that may offset future state taxable income through 2039. Current federal and state tax laws include substantial restrictions on the utilization of net operating losses and tax credits in the event of an ownership change. Even if the carryforwards are available, they may be subject to annual limitations, lack of future taxable income, or future ownership changes that could result in the expiration of the carryforwards before they are utilized. At December 31, 2019, we recorded a 100% valuation allowance against our deferred tax assets of approximately $245.0 million, as at that time our management believed it was uncertain that they would be fully realized. If we determine in the future that we will be able to realize all or a portion of our net operating loss carryforwards, an adjustment to valuation allowance would increase net income in the period in which we make such a determination.

In general, if we experience a greater than 50 percentage point aggregate change in ownership over a three-year period (a Section 382 ownership change), utilization of our pre-change NOL carryforwards are subject to an annual limitation under Section 382 of the Internal Revenue Code (California has similar laws). The annual limitation generally is determined by multiplying the value of our stock at the time of such ownership change (subject to certain adjustments) by the applicable long-term tax-exempt rate. Such limitations may result in expiration of a portion of the NOL carryforwards that were generated prior to 2018 before utilization. We have not utilized any NOL carryovers through December 31, 2019.

No liability related to uncertain tax positions is recorded on the consolidated financial statements. All uncertain tax positions are currently recorded as a reduction to our deferred tax asset. It is our policy to include

penalties and interest expense related to income taxes as a component of other expense and interest expense, respectively, as necessary.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2019	2018
Balance at beginning of year	$16,232	$11,150
Additions based on tax positions related to current year	5,366	5,144
Decreased for prior period positions	—	(62)
Unrecognized tax benefit—December 31	$21,598	$16,232

We do not expect that our uncertain tax positions will materially change in the next twelve months. The reversal of the uncertain tax benefits will not impact our effective tax rate as we continue to maintain a full valuation allowance against our deferred tax assets.

We file income tax returns in the United States, California and other states. We are not currently under examination by income tax authorities in federal, state or other jurisdictions. All tax returns will remain open for examination by the federal and state authorities for three and four years, respectively, from the date of utilization of any net operating loss or credits.

13. Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding for the period. Since we were in a loss position for all periods presented, diluted net loss per share is the same as basic net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive.

The following securities were not included in the diluted net loss per share calculations because their effect was anti-dilutive:

	December 31,		
	2019	2018	2017
Options to purchase common stock	3,573,860	3,243,551	2,945,901
Restricted shares subject to future vesting	—	47,051	241,617
Restricted stock units	1,848,772	975,419	820,713
Total	5,422,632	4,266,021	4,008,231

*****

Selected Quarterly Financial Information (unaudited)

The following table provides the selected consolidated quarterly financial data for 2019 and 2018:

	Quarter Ended							
(in thousands, except per share amounts)	December 31, 2019	September 30, 2019	June 30, 2019	March 31, 2019	December 31, 2018	September 30, 2018	June 30, 2018	March 31, 2018
Product sales, net	$ 2,108	$ —	$ —	$ —	$ —	$ —	$ —	$ —
Loss from operations	$ (99,214)	$ (68,742)	$(60,804)	$(52,523)	$ (52,084)	$ (45,476)	$(42,487)	$(42,695)
Net loss	$ (95,975)	$ (64,547)	$(57,321)	$(48,923)	$ (49,201)	$ (43,068)	$(40,368)	$(41,556)
Basic and diluted net loss per common share	$ (1.59)	$ (1.07)	$ (1.01)	$ (0.87)	$ (0.93)	$ (0.83)	$ (0.78)	$ (0.87)

Item 9. ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

None.

Item 9A. ***Controls and Procedures***

Evaluation of Disclosure Controls and Procedures

Our management carried out an evaluation, with the participation of our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. In connection with that evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures were effective. Disclosure controls and procedures means controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. These disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is accumulated and communicated to management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended). Our management, including our Chief Executive Officer and our Chief Financial Officer assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control—2013 Integrated Framework. Based on that assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2019. The effectiveness of our internal control over financial reporting as of December 31, 2019 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in its report which is included in Item 8 of this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Internal control over financial reporting may not prevent or detect all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Also, projections of any evaluation of effectiveness of internal control to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met.

Item 9B. ***Other Information***

None.

PART III

Item 10. ***Directors, Executive Officers and Corporate Governance***

Except as set forth below, the information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. The Code of Business Conduct and Ethics is posted on our website at https://www.ir.gbt.com.

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of The NASDAQ Stock Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Item 11. ***Executive Compensation***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

Item 13. ***Certain Relationships and Related Transactions and Director Independence***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

Item 14. ***Principal Accounting Fees and Services***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) The following documents are filed as part of this report:

(1) CONSOLIDATED FINANCIAL STATEMENTS

The consolidated financial statements filed as part of this Annual Report on Form 10-K are listed in the "Index to Consolidated Financial Statements" under Part II, Item 8 of this Annual Report on Form 10-K.

(2) CONSOLIDATED FINANCIAL STATEMENT SCHEDULES

Consolidated financial statement schedules have been omitted in this Annual Report on Form 10-K because they are not applicable, not required under the instructions, or the information requested is set forth in the consolidated financial statements or related notes thereto.

(3) EXHIBITS

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

Item 16. ***Form 10-K Summary***

None.

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Restated Certificate of Incorporation.	S-1/A	7/31/2015	3.2	
3.2	Amended and Restated Bylaws.	S-1/A	7/31/2015	3.4	
4.1	Specimen Common Stock Certificate.	S-1/A	7/31/2015	4.1	
4.2	Description of Securities	—	—	—	X
10.1#	2012 Stock Option and Grant Plan and forms of award agreements thereunder	S-1	7/8/2015	10.1	
10.2#	Amended and Restated 2015 Stock Option and Incentive Plan and forms of award agreements thereunder	S-8	1/23/2020	99.1	
10.3#	Employment Offer Letter Agreement by and between the Registrant and Ted W. Love, M.D., dated May 19, 2014	S-1	7/8/2015	10.3	
10.4#	Employment Offer Letter Agreement by and between the Registrant and Jeffrey Farrow, dated February 19, 2016	8-K	4/4/2016	10.1	
10.5	Form of Indemnification Agreement by and between the Registrant and each of its directors and officers	S-1/A	7/31/2015	10.8	
10.6#	2015 Employee Stock Purchase Plan	S-8	8/12/2015	99.3	
10.7#	Cash Incentive Bonus Plan	8-K	1/7/2020	10.2	
10.8#	Amended and Restated 2017 Inducement Equity Plan and forms of award agreements thereunder	S-8	1/23/2020	99.3	
10.9#	Employment Offer Letter by and between the Registrant and Patricia Suvari, dated October 7, 2016	10-K	3/13/2017	10.17	
10.10	Lease by and between the Company and HCP Oyster Point III LLC, dated March 17, 2017	8-K	3/22/2017	10.1	
10.11	Sales Agreement by and between the Company and Cowen and Company, LLC, dated August 23, 2017	S-3ASR	8/23/2017	1.2	
10.12#	Amended and Restated Severance and Change in Control Policy	8-K	1/9/2020	10.1	
10.13#	Employment Offer Letter by and between the Registrant and David Johnson, dated February 21, 2018	10-Q	5/7/2018	10.4	
10.14+	License Agreement by and between the Company and F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc., dated August 22, 2018	10-Q/A	3/29/2019	10.1	
10.15	First Amendment to Lease by and between the Company and HCP Oyster Point III LLC, dated August 29, 2018	8-K	8/30/2018	10.1	
10.16#	Non-Employee Director Compensation Policy	10-K	2/27/2019	10.18	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.17#	Employment Offer Letter by and between the Registrant and Brian Cathers, Ph.D., dated January 21, 2019	10-K	2/27/2019	10.19	
10.18#	Employment Offer Letter by and between the Registrant and Eric Fink, dated June 17, 2019	10-Q	8/7/2019	10.1	
10.19#	Employment Offer Letter by and between the Registrant and Jung Choi, dated March 16, 2015	10-Q	5/10/2019	10.1	
10.20+	License and Collaboration Agreement by and between the Registrant and Syros Pharmaceuticals, Inc., dated December 17, 2019	—	—	—	X
10.21+	Loan Agreement by and among the Registrant, BioPharma Credit PLC, and Biopharma Credit Investments V (Master) LP, dated December 17, 2019	—	—	—	X
21.1	Subsidiaries of the Registrant	—	—	—	X
23.1	Consent of KPMG LLP, Independent Registered Public Accounting Firm	—	—	—	X
24.1	Power of Attorney (included on signature page to this Annual Report)	—	—	—	X
31.1	Certification of Principal Executive Officer required by Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
31.2	Certification of Principal Financial Officer required by Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
32.1*	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
32.2*	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	—	—	—	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	—	—	—	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.	—	—	—	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.	—	—	—	X

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.	—	—	—	X
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.)	—	—	—	X

Represents management compensation plan, contract or arrangement.
+ Portions of this exhibit have been omitted as confidential information.
* The certifications attached as Exhibit 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the SEC and are not to be incorporated by reference into any filing of the registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

GLOBAL BLOOD THERAPEUTICS, INC.

By: /s/ Ted W. Love
Ted W. Love, M.D.
President and Chief Executive Officer (Principal Executive Officer)

Date: February 26, 2020

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Ted W. Love, M.D. and Jeffrey Farrow, and each of them, his true and lawful attorneys-in-fact, with full power of substitution, for him in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, hereby ratifying and confirming all that said attorneys-in-fact or any of them or their substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Ted W. Love Ted W. Love, M.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 26, 2020
/s/ Jeffrey Farrow Jeffrey Farrow	Chief Financial Officer *(Principal Financial Officer)*	February 26, 2020
/s/ Lesley A. Calhoun Lesley A. Calhoun	Senior Vice President of Finance and Chief Accounting Officer *(Principal Accounting Officer)*	February 26, 2020
/s/ Willie L. Brown, Jr. Willie L. Brown, Jr.	Director	February 26, 2020
/s/ Scott W. Morrison Scott W. Morrison	Director	February 26, 2020
/s/ Mark L. Perry Mark L. Perry	Director	February 26, 2020
/s/ Glenn F. Pierce Glenn F. Pierce, M.D., Ph.D.	Director	February 26, 2020
/s/ Philip A. Pizzo Philip A. Pizzo, M.D.	Director	February 26, 2020

Signature	Title	Date
/s/ Dawn Svoronos Dawn Svoronos	Director	February 26, 2020
/s/ Wendy Yarno Wendy Yarno	Director	February 26, 2020

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of December 31, 2019, Global Blood Therapeutics, Inc. (the "Company," "we," "us," and "our") had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended: our Common Stock.

Description of Common Stock

The following description of our Common Stock is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our Restated Certificate of Incorporation ("Certificate of Incorporation") and our Amended and Restated Bylaws ("Bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.2 is a part, and by applicable law. We encourage you to read our Certificate of Incorporation, our Bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

Authorized Capital Stock

Our authorized capital stock consists of 150,000,000 shares of common stock, par value $0.001 per share (the "Common Stock"), and 5,000,000 shares of preferred stock, par value $0.001 per share (the "Preferred Stock"), all of which shares of Preferred Stock are undesignated.

Common Stock

The holders of our Common Stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our Common Stock do not have any cumulative voting rights. Holders of our Common Stock are entitled to receive ratably any dividends declared by our board of directors (the "Board") out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding Preferred Stock. Our Common Stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions. In the event of our liquidation, dissolution or winding up, holders of our Common Stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding Preferred Stock. All outstanding shares are fully paid and nonassessable.

Our Common Stock is listed on The Nasdaq Global Select Market under the symbol "GBT."

The transfer agent and registrar for our Common Stock is Continental Stock Transfer and Trust Company.

Preferred Stock — Limitations on Rights of Holders of Common Stock

Our Board is authorized to issue up to 5,000,000 shares of undesignated Preferred Stock in one or more series without stockholder approval. Our Board may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of Preferred Stock. The purpose of authorizing our Board to issue Preferred Stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. Examples of rights and preferences that the Board may fix are: dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of our Common Stock. The rights of holders of our Common Stock will be subject to, and may be adversely affected by, the rights of any Preferred Stock that we may designate and issue in the future. The issuance of shares of undesignated Preferred Stock could decrease the amount of earnings and assets available for distribution to holders of shares of Common Stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Antitakeover Effects of Delaware Law and Provisions of our Certificate of Incorporation and Bylaws

Certain provisions of the Delaware General Corporation Law and of our Certificate of Incorporation and Bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our Common Stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our Board. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our Common Stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our Board approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our Board and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Provisions of our Certificate of Incorporation and Bylaws

Our Certificate of Incorporation and Bylaws include a number of provisions that may have the effect of delaying, deferring or discouraging another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our Board rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies. In accordance with our Certificate of Incorporation, our Board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our Certificate of Incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our Board, however occurring, including a vacancy resulting from an increase in the size of our Board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No written consent of stockholders. Our Certificate of Incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our Bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of stockholders. Our Bylaws provide that only a majority of the members of our Board then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our Bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements. Our Bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our Bylaws.

Amendment to Certificate of Incorporation and Bylaws. As required by the Delaware General Corporation Law, any amendment of our Certificate of Incorporation must first be approved by a majority of our Board, and if required by law or our Certificate of Incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our Certificate of Incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our Bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the Bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the Board recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Exhibit 10.20

CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED. SUCH EXCLUDED INFORMATION HAS BEEN MARKED WITH "[***]".

Execution Copy

LICENSE AND COLLABORATION AGREEMENT

by and between

SYROS PHARMACEUTICALS, INC.

and

GLOBAL BLOOD THERAPEUTICS, INC.

Dated as of December 17, 2019

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LICENSE AND COLLABORATION AGREEMENT

This **LICENSE AND COLLABORATION AGREEMENT** (this "**Agreement**") is made as of December 17, 2019 (the "**Effective Date**"), by and between **Syros Pharmaceuticals, Inc.**, a Delaware corporation ("**Syros**"), having its principal office at 35 CambridgePark Drive, Cambridge, MA 02140, and **Global Blood Therapeutics, Inc.**, a Delaware corporation ("**GBT**"), having its principal office at 171 Oyster Point Blvd, Suite 300, South San Francisco, CA 94080. GBT and Syros are referred to in this Agreement individually as a "**Party**" and collectively as the "**Parties**".

RECITALS

WHEREAS, Syros is a biopharmaceutical company focused on discovering, researching and developing small-molecule drugs to control the expression of genes;

WHEREAS, GBT is a commercial biotechnology company focused on discovering, developing and commercializing therapies to address unmet medical needs; and

WHEREAS, Syros and GBT desire to collaborate in target identification and validation and the discovery and development of candidate compounds directed to selected targets that induce fetal hemoglobin, and Syros desires to grant GBT an exclusive option to obtain an exclusive license to further develop and commercialize such compounds, all under the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants contained herein, the receipt and sufficiency of which are hereby acknowledged, GBT and Syros hereby agree as follows:

ARTICLE 1
DEFINITIONS

Unless the context otherwise requires, the terms in this Agreement with initial letters capitalized will have the meanings set forth below, or the meanings as designated in the indicated places throughout this Agreement.

1.1 "**Active Ingredient**" means any clinically active material that provides pharmacological activity in a pharmaceutical product (excluding formulation components such as coatings, stabilizers, excipients or solvents, adjuvants or controlled release technologies).

1.2 "**Affiliate**" means, with respect to a Party, any Person that controls, is controlled by, or is under common control with that Party. For the purpose of this definition, "control" (including, with correlative meaning, the terms "controlled by" and "under common control") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of a Person, whether by the ownership of at least fifty percent (50%) of the voting stock of such Person, by contract or otherwise.

1.3 "**Agreement**" is defined in the preamble hereto.

1.4 "**Alliance Manager**" is defined in Section 4.9.

1.5 "**Antitrust Approval**" means any consent, approval or other authorization required under the applicable Antitrust Laws from the applicable Antitrust Authority.

1.6 "**Antitrust Authority**" means any applicable Governmental Authority with respect to any Antitrust Laws.

1.7 "**Antitrust Condition**" means that (a) the waiting period (and any extension thereof) applicable to GBT's exercise of the Option under any and all applicable Antitrust Laws, shall have expired or been terminated, and (b) if applicable, any applicable Antitrust Approval for exercise of the Option under such Antitrust Laws has been received.

1.8 "**Antitrust Filing**" means a filing or filings by the Parties with the applicable Antitrust Authority as required by the Antitrust Laws with respect to GBT's exercise of the Option together with all required documentary attachments thereto.

1.9 "**Approved Costs**" is defined in Section 6.2.

1.10 "**Backup Compound**" is defined in Section 6.4(b).

1.11 "**Business Day**" means a day other than Saturday, Sunday or any other day on which banking institutions in New York, New York are closed for business.

1.12 "**Change of Control**" means, with respect to a Party, the occurrence of any of the following events: (a) such Party sells, conveys or otherwise disposes of all or substantially all of its assets; (b) a merger, reorganization or consolidation involving such Party or any direct or indirect parent of such Party in which the voting securities of such Party, or any direct or indirect parent of such Party, outstanding immediately prior thereto cease to represent more than fifty percent (50%) of the combined voting power of the surviving entity immediately after such merger, reorganization or consolidation; or (c) a Person, or group of Persons acting in concert, acquire, directly or indirectly, more than fifty percent (50%) of the voting equity securities or management control of such Party.

1.13 "**Claims**" is defined in Section 9.1.

1.14 "**Co-Detail Product**" is defined in Section 5.8(a).

1.15 "**Co-Detail Start Date**" is defined in Section 5.8(d)(i).

1.16 "**Co-Detailing Agreement**" is defined in Section 5.8(c).

1.17 "**Co-Detailing Option**" is defined in Section 5.8(a).

1.18 "**Co-Detailing Option Exercise Fee**" means [***] Dollars ($[***]).

1.19 "**Collaboration Compound**" means any Compound identified, synthesized or developed by or on behalf of either Party (or jointly by or on behalf of the Parties) in the conduct

of the Research Program that modulates one or more Collaboration Targets as its primary mechanism of action, as demonstrated in an in vitro assay determined by the JSC as appropriate for such determination.

1.20 "**Collaboration Target**" means (a) subject to Sections 4.1(f) and 4.2, each biological target set forth on **Exhibit C**, (b) each other biological target that induces fetal hemoglobin and that the JSC agrees by consensus to add to the Research Program (subject to the mechanism described in Section 4.2), (c) any portion or fragment of any biological target in (a) or (b), (d) any naturally occurring variant of any biological target in (a), (b) or (c), including any mutated form or any post-translationally modified form of any of the foregoing, (e) any co-factor associated with any biological target in (a), (b), (c) or (d), and (e) any nucleic acid encoding any biological target in (a), (b), (c) or (d).

1.21 "**Collaboration Target Validation Activities**" is defined in Section 3.6(a)(ii).

1.22 "**Combination Product**" means: (a) a pharmaceutical product that consists of a Licensed Compound and at least one other Active Ingredient that is not a Licensed Compound; or (b) any combination of a Product and another pharmaceutical product that contains at least one other Active Ingredient that is not a Licensed Compound, where such products are not formulated together but are sold together as a single product and invoiced for a single price. The other Active Ingredient(s) in clause (a) and the other pharmaceutical product(s) in clause (b) are each referred to as the "**Other Product(s)**".

1.23 "**Commercialize**" or "**Commercialization**" means all activities directed to marketing, promoting, distributing, detailing or selling a Product (as well as importing and exporting activities in connection therewith), including the commercial manufacture of Licensed Compounds and Products.

1.24 "**Commercially Reasonable Efforts**" means, with respect to each Party's obligations under this Agreement to research, Develop or Commercialize a Compound or Product, [***].

1.25 "**Committee**" means, individually and collectively, the JSC and the JDC.

1.26 "**Competing Compound**" means any Compound, other than a Licensed Compound.

1.27 "**Competitive Drug Discovery Program**" is defined in the definition of "Competitive Program".

1.28 "**Competitive Program**" means a program to conduct (a) the clinical development or commercialization of any Competing Compound, or (b) Collaboration Target Validation Activities or (c) Drug Discovery and Development Activities with the specific intent to discover or develop any Competing Compound (any program under clause (c), a "**Competitive Drug Discovery Program**").

1.29 "**Competitive Program Transaction**" is defined in Section 3.6(b).

1.30 "**Compound**" means any compound that modulates one or more Collaboration Targets as its primary mechanism of action.

1.31 "**Confidential Information**" of a Party means all Know-How, unpublished patent applications and other information and data of a financial, commercial, business, operational, technical or other proprietary nature of such Party that is disclosed by or on behalf of such Party or any of its Affiliates or otherwise made known to the other Party or any of its Affiliates, whether disclosed or made known orally, in writing or in electronic form pursuant to this Agreement; provided that (x) all Inventions or Program Know-How will be deemed (i) Syros' Confidential Information prior to the Option Effective Date, and Syros shall be deemed to be the Disclosing Party and GBT shall be deemed to be the Receiving Party with respect thereto and (ii) the Confidential Information of both Parties following the Option Effective Date, and both Parties shall be deemed to be the Receiving Party and the Disclosing Party with respect thereto; (y) all Syros Platform Improvements will be deemed Syros' Confidential Information, and Syros shall be deemed to be the Disclosing Party and GBT shall be deemed to be the Receiving Party with respect thereto; and (z) the terms of this Agreement will be deemed the Confidential Information of both Parties, and both Parties shall be deemed to be the Receiving Party and the Disclosing Party with respect thereto.

1.32 "**Confidentiality Agreement**" means that certain confidentiality agreement between the Parties, dated August 8, 2019.

1.33 "**Control**" or "**Controlled**" means, with respect to any Regulatory Materials, Know-How, Patent Rights or other intellectual property rights, that a Party has the legal authority or right (whether by ownership, license or otherwise) to grant a license, sublicense or other right (as applicable) under such Regulatory Materials, Know-How, Patent Rights, or other intellectual property rights to the other Party on the terms and conditions set forth herein, in each case without breaching the terms of any agreement with a Third Party.

1.34 "**Covering Claim**" is defined in Section 1.123.

1.35 "**Develop**" or "**Development**" means all development activities for any Licensed Compound or Product, including all preclinical studies, clinical testing, manufacturing development, process development, toxicology studies, manufacturing and distribution of Product for use in clinical trials (including placebos and comparators), statistical analyses, and the preparation, filing, prosecution of, and seeking approval for, any IND or any Marketing Approval Application for any Product, as well as all regulatory affairs related to any of the foregoing.

1.36 "**Disclosing Party**" is defined in Section 10.1(a).

1.37 "**Disputes**" is defined in Section 12.7.

1.38 "**Dollar**" means U.S. dollars, and "$" shall be interpreted accordingly.

1.39 "**Drug Discovery and Development Activities**" is defined in Section 3.6(a)(ii).

1.40 "**Effective Date**" is defined in the preamble hereto.

1.41 "**EMA**" means the European Medicines Agency or any successor entity thereto.

1.42 "**Excluded Transaction IP**" is defined in Section 12.3(b).

1.43 "**Exclusivity Period**" is defined in Section 3.6(a)(i).

1.44 "**Executive Officers**" means with respect to Syros, its Chief Executive Officer or his or her designee, and with respect to GBT, its Chief Executive Officer or his or her designee.

1.45 "**Exercise Notice**" is defined in Section 5.8(b).

1.46 "**FDA**" means the United States Food and Drug Administration or any successor entity thereto.

1.47 "**Field**" means any and all uses.

1.48 "**First-in-Human Clinical Trial**" means, in respect of a Product, a clinical study of such Product in healthy human volunteers (as distinct from patients) that is designed to make a preliminary determination of the safety, pharmacokinetic and pharmacodynamic parameters for such Product.

1.49 "**First-in-Patient Clinical Trial**" means, in respect of a Product, a clinical study of such Product in a target patient population for such Product that is designed to establish safety and pharmacokinetic and pharmacodynamic parameters, and which may also be designed to establish an initial indication of efficacy.

1.50 "**First Commercial Sale**" means, with respect to any Product in any country or jurisdiction in the Territory, the first sale of such Product to a Third Party for distribution, use or consumption in such country or jurisdiction after Regulatory Approval has been obtained for such Product in such country or jurisdiction.

1.51 "FTE" means the equivalent of a full-time employee's work for a twelve (12)-month period (consisting of a total of [***] hours per year of dedicated effort), conducting activities under the Research Plan. In no event shall any one individual be counted as more than one (1) FTE.

1.52 "**FTE Rate**" means [***] Dollars ($[***]) per FTE per year.

1.53 "**GAAP**" means U.S. generally accepted accounting principles.

1.54 "**GBT**" is defined in the preamble hereto.

1.55 "**GBT Indemnitees**" is defined in Section 9.1.

1.56 "**GBT Licensed IP**" means all Patent Rights and Know-How that are (a) Controlled by GBT or its Affiliates as of the Effective Date or thereafter during the Term and (b) reasonably necessary for Syros to conduct its activities under the Research Plan.

1.57 "**GBT Sole Inventions**" means any Sole Inventions that are conceived or otherwise made solely by or on behalf of GBT or any of its Affiliates.

1.58 "**GBT Sole Know-How**" means any Program Know-How that is conceived, discovered, generated or otherwise made solely by or on behalf of GBT or any of its Affiliates.

1.59 "**GBT Sole Patents**" means all Patent Rights solely claiming patentable Sole Inventions of GBT.

1.60 "**GLP**" or "**Good Laboratory Practices**" means the then-current good laboratory practice standards promulgated or endorsed by the FDA as defined in 21 C.F.R. Part 58, and comparable regulatory standards promulgated by the EMA or other Regulatory Authority applicable to the Territory, as they may be updated from time to time, including applicable quality guidelines promulgated under the ICH.

1.61 "**GMP**" or "**Good Manufacturing Practices**" means the current good manufacturing practices applicable from time to time to the manufacturing of a Licensed Compound or a Product or any intermediate thereof pursuant to applicable Law.

1.62 "**Governmental Authority**" means any federal, state, national, provincial or local government, or political subdivision thereof, or any multinational organization or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, or any court or tribunal (or any department, bureau or division thereof, or any governmental arbitrator or arbitral body).

1.63 "**Incurred Budgeted Costs**" is defined in Section 6.2.

1.64 "**IND**" means any investigational new drug application, clinical trial application, clinical trial exemption or similar or equivalent application or submission for approval or authorization to conduct a human clinical investigation filed with or submitted to a Regulatory Authority in conformance with the requirements of such Regulatory Authority.

1.65 "**IND-Enabling Studies**" means those studies that are reasonably required to meet the requirements for filing an IND with a Regulatory Authority, including GLP toxicology and safety studies, or studies required for the preparation of the CMC section of such IND.

1.66 "**IND Candidate**" means any Collaboration Compound that has been determined by GBT to be a candidate for commencement of IND-Enabling Studies pursuant to Section 2.4(a).

1.67 "**Indemnified Party**" is defined in Section 9.3.

1.68 "**Indemnifying Party**" is defined in Section 9.3.

1.69 "**Indication**" means a separate and distinct disease, disorder or condition in humans: (a) which a Product is intended to treat or prevent, as evidenced by the protocol for a clinical trial of such Product or by the proposed Product labeling in an MAA filed with a Regulatory Authority for such Product; or (b) which is contained in a Product's labeling approved by a Regulatory Authority as part of the Regulatory Approval for such Product, it being understood that: (i) the treatment or prevention of separate varieties of the same disease, disorder or condition (*e.g.*, acute vs. chronic) shall not be treated as separate Indications; (ii) the treatment or prevention of the same disease, disorder or condition in different populations (*e.g.*, adult and pediatric; or treatment-naïve and relapsed/refractory) shall not be treated as separate Indications; and (iii) prevention of a disease, disorder or condition shall not be treated as a separate Indication from treatment of the same disease, disorder or condition. Furthermore, a label enhancement or elaboration or expansion of an approved Indication is not a separate Indication even if one or more clinical trials are performed to receive such enhancement or elaboration. For the avoidance of doubt, sickle cell disease and beta thalassemia are distinct Indications.

1.70 "**Infringement**" is defined in Section 7.6(c)(i).

1.71 "**Initial Research Term**" is defined in Section 2.3(a).

1.72 "**Initiation**" means, with respect to a clinical trial of a Product, the first dosing of the first human subject in such clinical trial.

1.73 "**Invention**" means any inventions (whether patentable or not) that are conceived or otherwise made (a) by or on behalf of a Party or its Affiliates, whether solely or jointly with any Third Party (or with the other Party or its Affiliates) under or in connection with the conduct of the Research Program, or (b) by or on behalf of GBT or its Affiliates, whether solely or jointly, in connection with exercising its rights under the evaluation license granted pursuant to Section 2.1; excluding in each case ((a) and (b)) any Syros Excluded IP.

1.74 "**IFRS**" means International Financial Reporting Standards.

1.75 "**Joint Inventions**" means any Inventions that are conceived or otherwise made jointly by or on behalf of one Party or any of its Affiliates and the other Party or any of its Affiliates, as determined in accordance with Section 7.1(a).

1.76 "**Joint IP**" means all Joint Inventions, Joint Patents and Joint Know-How.

1.77 "**Joint Know-How**" means any Program Know-How that is conceived, discovered generated or otherwise made jointly by or on behalf of one Party or any of its Affiliates and the other Party or any of its Affiliates.

1.78 "**Joint Patents**" means all Patent Rights claiming patentable Joint Inventions.

1.79 "**Joint Development Committee**" or "**JDC**" is defined in Section 4.5.

1.80 "**Joint Steering Committee**" or "**JSC**" is defined in Section 4.1.

1.81 "**Know-How**" means any scientific or technical information, including discoveries, improvements, modifications, processes, methods, protocols, formulas, data, inventions, know-how and trade secrets, patentable or otherwise, but excluding any of the foregoing claimed in any Patent Rights and excluding any Regulatory Materials.

1.82 "**Law**" means any federal, state, local, foreign or multinational law, statute, standard, ordinance, code, rule, regulation, resolution or promulgation, or any order by any Governmental Authority, or any license, franchise, permit or similar right granted under any of the foregoing, or any similar provision having the force or effect of law.

1.83 "**Licensed Compound**" means (a) any Collaboration Compound, (b) any Select Related Compound, and (c) any metabolite, salt, hydrate, solvate, enantiomer, free acid form, free base form, ester, deuterated form, crystalline form, co-crystalline form, amorphous form, pro drug form, racemate, polymorph, chelate, stereoisomer, tautomer, or optically active form of any compound in the preceding clause (a) or (b).

1.84 "**Licensed Covering Claim**" means a Covering Claim in a Licensed Patent.

1.85 "**Licensed IP**" means all Licensed Patents and Licensed Know-How.

1.86 "**Licensed Know-How**" means (a) all Know-How that is (i) Controlled by Syros or its Affiliates as of the Effective Date, and (ii) necessary or useful for the research, Development, manufacture or Commercialization of Licensed Compounds or Products, and (b) without limitation to clause (a), Syros Sole Know-How, Syros Sole Inventions and Syros' interests in any Joint Know-How and Joint Inventions; excluding in each case ((a) and (b)) Syros Excluded IP.

1.87 "**Licensed Patents**" means the Syros Sole Patents, any Other Syros Patents, and Syros' interest in any Joint Patents.

1.88 "**Losses**" is defined in Section 9.1.

1.89 "**MAA**" or "**Marketing Authorization Application**" means an application to the appropriate Regulatory Authority for approval to commercially sell a Product in a particular jurisdiction, and all amendments and supplements thereto, including an NDA in the United States.

1.90 "**Major Market**" means any of the United Kingdom, Germany, France, Italy and Switzerland.

1.91 "**Materials**" is defined in Section 2.9.

1.92 "**NDA**" means a New Drug Application, as defined in the U.S. Federal Food, Drug & Cosmetic Act, as amended, and applicable regulations promulgated thereunder by the FDA, including 21 C.F.R. Part 314.

1.93 "**Net Sales**" means, with respect to any Product, in a particular period, the sum of (a) and (b) below:

(a) the amount stated in GBT's "sales" line of its audited financial statements with respect to such Product for such period (excluding sales to any Third Party sublicensees, unless these sublicensees are the final end-user). This amount reflects the gross invoice price at which such Product was sold or otherwise disposed of by GBT and its Affiliates to Third Parties (excluding sales to any Third Party sublicensees, unless these sublicensees are the final end-user) in such period reduced by gross-to-net deductions, if not previously deducted from such invoiced amount, taken in accordance with the then-currently used IFRS or GAAP, as applicable. By way of example, the gross-to-net deductions taken in accordance with GAAP as of the Effective Date may include but are not limited to the following:

(i) credits, reserves or allowances granted for (A) damaged, outdated, returned, rejected, withdrawn or recalled Product, (B) wastage replacement and short-shipments, (C) billing errors, and (D) indigent patient, patient assistance and/or reimbursement, access-to-care and similar programs (*e.g.*, price capitation);

(ii) governmental price reductions and government mandated rebates;

(iii) chargebacks, including those granted to wholesalers, buying groups and retailers; and

(iv) customer rebates, including cash sales incentives for prompt payment, cash and volume discounts.

Notwithstanding the foregoing, if the amount stated in GBT's "sales" line of its audited financial statements is not reported on a Product-by-Product basis with respect to any period, the amount pursuant to this clause (a) shall instead equal, with respect to a Product for any period, the gross amount invoiced by GBT and its Affiliates to Third Parties for the sale of such Product (excluding sales to any Third Party sublicensees, unless these sublicensees are the final end-user) less deductions with respect to such Product for such period pursuant to subclauses (i) through (iv) of this clause (a) and any other reasonable and customary deductions, if not previously deducted from such invoiced amount, taken in accordance with the then-currently used IFRS or GAAP, as applicable.

(b) for Third Party sublicensees, the net sales amounts reported to GBT or its Affiliates in accordance with this Agreement and their then-currently used IFRS or GAAP, as applicable.

Notwithstanding the foregoing, amounts received or invoiced by GBT or its Affiliates or sublicensees for the sale of Products among GBT and its Affiliates and sublicensees shall not be included in the computation of Net Sales hereunder.

Net Sales shall not include any amounts invoiced for Products supplied for use in clinical trials or under early access, compassionate use, samples, named patient, indigent or low resource country access, patient assistance or other reduced pricing programs.

For purposes of determining the royalties and milestones due under this Agreement, Net Sales for a Combination Product in a country shall be calculated as follows:

(i) [***].

(ii) [***].

(iii) [***].

(iv) [***].

1.94 "**Notice of Conditional Exercise**" is defined in Section 3.1(d)(i).

1.95 "**Option**" is defined in Section 3.1(a).

1.96 "**Option Effective Date**" is defined in Section 3.2(a).

1.97 "**Option Exercise Fee**" is defined in Section 6.3.

1.98 "**Option Exercise Notice**" is defined in Section 3.1(b).

1.99 "**Option Exercise Period**" is defined in Section 3.1(c).

1.100 "**Other Product**" is defined in Section 1.22.

1.101 "**Other Royalty Patent**" means any and all Patent Rights that (a) are owned or controlled by GBT or its Affiliates or its or their sublicensees during the Term and (b) cover or claim the composition of any Select Related Compound, including any such Patent Rights within the GBT Sole Patents. For clarity, the Other Royalty Patents do not include Patent Rights to the

extent claiming manufacturing processes, dosing, methods of treatment or use, or any formulation or drug delivery technology used with any Select Related Compounds.

1.102 "**Other Syros Patents**" means any Patent Rights that ((a), (b) and (c)): (a) are Controlled by Syros or its Affiliates as of the Effective Date, (b) cover or claim the Development, manufacture or Commercialization of any Licensed Compound or Product and (c) are not Syros Sole Patents or Joint Patents; excluding any Syros Excluded IP.

1.103 "**Party**" and "**Parties**" are defined in the preamble hereto.

1.104 "**Patent Rights**" means all patents and patent applications (which for the purpose of this Agreement shall be deemed to include certificates of invention and applications for certificates of invention), including all divisionals, continuations, substitutions, continuations-in-part, re-examinations, reissues, additions, renewals, revalidations, extensions, registrations, pediatric exclusivity periods and supplemental protection certificates and the like of any such patents and patent applications, and any and all foreign equivalents of the foregoing.

1.105 "**Permitted Lien**" means any lien, security interest, pledge, assessment, charge or other similar right or interest granted by a Party to any Third Party in connection with any lending transaction.

1.106 "**Permitted Overspend**" is defined in Section 2.5.

1.107 "**Person**" means any individual, partnership, limited liability company, firm, corporation, association, trust, unincorporated organization or other entity.

1.108 "**Phase 3 Clinical Trial**" means, in respect of a Product, a human clinical trial that is prospectively designed, together with prior data, to demonstrate statistically whether such Product is safe and effective for use in humans in a manner sufficient to obtain approval of the MAA to market such Product in patients having the disease, disorder or condition being studied as described in 21 C.F.R. § 312.21(c), as may be amended from time to time**,** and the foreign equivalents thereof.

1.109 "**Pricing Approval**" means, in respect of a Product, such governmental approval, agreement, determination or decision establishing prices for such Product that can be charged and/or reimbursed in regulatory jurisdictions where the applicable Governmental Authorities approve or determine the price and/or reimbursement of pharmaceutical products.

1.110 "**Product**" means any pharmaceutical product that contains a Licensed Compound as an Active Ingredient, alone or in combination with one or more other Active Ingredients, in any and all forms, presentations, formulations, and dosage forms.

1.111 "**Product Marks**" is defined in Section 7.10.

1.112 "**Program Know-How**" any Know-How (other than Inventions) that is conceived, discovered, generated or otherwise made (a) by or on behalf of a Party or its Affiliates, whether solely or jointly with any Third Party (or with the other Party or its Affiliates) under or in connection with the conduct of the Research Program, or (b) by or on behalf of GBT or its

Affiliates, solely or jointly with any Third Party, in connection with exercising its rights under the evaluation license granted pursuant to Section 2.1; excluding in each case ((a) and (b)) any Syros Excluded IP.

1.113 "**Receiving Party**" is defined in Section 10.1(a).

1.114 "**Registrational Clinical Trial"** means, in respect of a Product, either (a) a Phase 3 Clinical Trial for such Product or (b) a registration trial sufficient for filing an MAA for such Product with the FDA or the EMA as evidenced by (i) an agreement with, or statement from, the FDA or the EMA on a special protocol assessment or its equivalent, or (ii) other guidance or minutes issued by the FDA or EMA, for such registration trial.

1.115 "**Regulatory Approval**" means, in respect of a Product and a country or regulatory jurisdiction, approval of the MAA for such Product and country or regulatory jurisdiction and all other approvals, including, for clarity, Pricing Approvals, that are necessary for the commercial sale of such Product in such country or regulatory jurisdiction.

1.116 "**Regulatory Authority**" means any applicable Governmental Authority responsible for granting Regulatory Approvals for Products, including the FDA, EMA and any corresponding national or regional regulatory authorities.

1.117 "**Regulatory Exclusivity**" means, in respect of a Product and a country or jurisdiction, any exclusive marketing rights or data exclusivity rights (other than Patent Rights) conferred by any Regulatory Authority or by applicable Law with respect to such Product in such country or jurisdiction, including for clarity that prevent another Person from using or otherwise relying on any data supporting the approval of the MAA for such Product to support an application for regulatory approval of another product for any indication without the prior written consent of the MAA holder, including orphan drug exclusivity, new chemical entity exclusivity, new product or use exclusivity and pediatric exclusivity.

1.118 "**Regulatory Materials**" means any regulatory application, submission, notification, communication, correspondence, meeting minutes, registration and other filings made to, received from or otherwise conducted with a Regulatory Authority with respect to a Licensed Compound or Product in order to Develop, manufacture, market, sell or otherwise Commercialize such Licensed Compound or Product in a particular country or jurisdiction. Regulatory Materials includes any IND or MAA.

1.119 "**Research Budget**" is defined in Section 2.2.

1.120 "**Research Plan**" is defined in Section 2.2.

1.121 "**Research Program**" is defined in Section 2.1.

1.122 "**Research Term**" is defined in Section 2.3(b).

1.123 "**Royalty Term**" means, with respect to a Product and country, the period commencing upon the First Commercial Sale of such Product in such country and ending upon the latest of: (a) ten (10) years after such First Commercial Sale of such Product in such country; (b)

the expiration of the last-to-expire Valid Claim in the Licensed Patents and Other Royalty Patents that would be infringed, absent a license thereunder or ownership thereof (considering patent applications to be issued with the then-pending claims), by the sale or approved use of such Product in such country (a "**Covering Claim**" for such Product and country); and (c) the expiration of Regulatory Exclusivity for such Product in such country.

1.124 "Select Related Compound" means any Compound (other than a Collaboration Compound) that modulates one or more Collaboration Targets as its primary mechanism of action, as demonstrated in an *in vitro* assay determined by the JSC, and (a) is claimed (including in a genus claim) or disclosed in any Patent Right within (i) the Syros Sole Patents or (ii) the Joint Patents or (b) is identified, synthesized or developed by or on behalf of GBT or its Affiliates during the Research Term (including, for clarity, after Option Exercise if Option Exercise occurs during the Research Term, if any).

1.125 "**Sole Inventions**" means any Inventions invented or otherwise made solely by or on behalf of a Party or its Affiliates, as determined in accordance with Section 7.1(a).

1.126 "**Syros**" is defined in the preamble hereto.

1.127 "Syros Excluded IP" means Know-How, Inventions, Patent Rights or other intellectual property rights owned or controlled by Syros or its Affiliates that cover, claim or constitute (a) the Syros Platform or the Syros Platform Improvements (such Know-How, Inventions, Patent Rights and other intellectual property rights, collectively, the "**Syros Platform IP**"), (b) manufacturing, formulation or drug delivery technology of Syros or any of its Affiliates that is not used by or on behalf of Syros or its Affiliates in the manufacture or supply of any Licensed Compound or Product during the Research Term or pursuant to any supply agreement entered into by the Parties pursuant to Section 5.6(b), and (c) any compound other than any Licensed Compound or any product other than a Product; provided that the Syros Excluded IP excludes any Patent Rights that cover or claim, or Know-How that constitutes, the composition of matter or method of use of any Licensed Compound.

1.128 "**Syros Indemnitees**" is defined in Section 9.2.

1.129 "**Syros Platform**" means Syros' proprietary gene control platform for the discovery and development of small molecule therapeutics owned or controlled by Syros as of the Effective Date or developed thereafter independent of this Agreement, consisting of regulatory genomics, disease biology, and small molecule transcriptional chemistry capabilities, including instruments, analytical methods, algorithms, databases of regulatory genomes, procedures, reagents, techniques, software, and compound structure discovery, screening and assay technologies. For clarity, the Syros Platform does not include the composition of matter or method of use of any Compound.

1.130 "**Syros Platform Improvement**" means any modification or improvement to those aspects of the Syros Platform that are used, practiced or disclosed in connection with the Research Program, which modification or improvement is made by or on behalf of either Party or its Affiliates, solely or jointly, in connection with the Research Program.

1.131 "**Syros Platform IP**" is defined in the definition of Syros Excluded IP.

1.132 "Syros Platform Patents" means Patent Rights within the Syros Platform IP.

1.133 "Syros Sole Inventions" means any Sole Inventions that are conceived or otherwise made solely by or on behalf of Syros or any of its Affiliates.

1.134 "**Syros Sole Know-How**" means any Program Know-How that is conceived, discovered, generated or otherwise made solely by or on behalf of Syros or any of its Affiliates.

1.135 "**Syros Sole Patents**" means all Patent Rights solely claiming patentable Syros Sole Inventions.

1.136 "**Term**" is defined in Section 11.1.

1.137 "**Territory**" means the world.

1.138 "**Third Party**" means any Person other than a Party or an Affiliate of a Party.

1.139 "**Third Party Payments**" is defined in Section 7.9.

1.140 "**Transfer Date**" is defined in Section 7.2.

1.141 "**Unapproved Costs**" is defined in Section 6.2.

1.142 "**United States**" or "**U.S.**" means the United States of America, including its territories and possessions.

1.143 "**Utilized Syros Platform IP**" is defined in Section 3.7.

1.144 "**Valid Claim**" means a claim of (a) an issued and unexpired patent (as may be extended through supplementary protection certificate or patent term extension or the like) that has not been revoked or held invalid or unenforceable by a patent office, court or other governmental agency of competent jurisdiction in a final and non-appealable judgment (or judgment from which no appeal was taken within the allowable time period) and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise, or (b) a pending patent application that (i) has been pending less than [***] from its earliest priority date, (ii) was filed and is being prosecuted in good faith and (iii) has not been cancelled, withdrawn or abandoned or finally rejected by an administrative agency action from which no appeal can be taken.

1.145 "**[***]**" is defined in Section 3.7.

1.146 Interpretation. This Agreement has been prepared in the English language, and the English language shall control its interpretation. In this Agreement, unless otherwise specified:

(a) "include", "includes" and "including" shall be deemed to be followed by the phrase "without limitation";

(b) the word "or" shall not be construed as exclusive;

(c) references to any Articles or Sections include Articles, Sections and subsections that are part of the related Article or Section;

(d) words denoting the singular shall include the plural and vice versa, and words denoting any gender shall include all genders;

(e) words such as "herein", "hereof" and "hereunder" refer to this Agreement as a whole and not merely to the particular provision in which such words appear; and

(f) the Exhibits and other attachments form part of the operative provision of this Agreement, and references to this Agreement shall include references to the Exhibits and attachments.

ARTICLE 2
RESEARCH PROGRAM

2.1 General; License Grants for Conduct of Research Plan. Subject to the terms and conditions of this Agreement, Syros shall utilize aspects of the Syros Platform and, if applicable, the Syros Platform Improvements in conducting, and the Parties shall undertake a research collaboration during the Research Term to identify and validate Collaboration Targets and to discover, identify and pre-clinically develop Collaboration Compounds, under the Research Plan and, subject to Section 2.5, consistent with the Research Budget and under the oversight of the JSC, with the goal of identifying at least one IND Candidate (the "**Research Program**"). GBT has the Option described in Section 3.1 to obtain an exclusive license for further Development and Commercialization by GBT of Licensed Compounds and Products in the Field and in the Territory. Subject to the terms and conditions of this Agreement, Syros hereby grants to GBT a non-exclusive license, without the right to grant sublicenses, under the Licensed IP, solely to conduct the activities allocated to GBT under the Research Plan during the Research Term, in accordance with the terms of this Agreement, and to evaluate Collaboration Compounds during the Research Term and any additional period in which the Option Exercise Period remains in effect. Subject to the terms and conditions of this Agreement, GBT hereby grants to Syros a non-exclusive license, without the right to grant sublicenses, under the GBT Licensed IP solely to conduct the activities allocated to Syros under the Research Plan during the Research Term, in accordance with the terms of this Agreement.

2.2 Research Plan and Budget. The Parties shall conduct their activities during the Research Term in accordance with a written research plan that: (a) allocates research responsibilities between the Parties; (b) sets forth the details and anticipated timing of the research activities to be conducted by each Party; and (c) specifies the number and function of Syros FTEs conducting activities (the "**Research Plan**"). The Research Plan will include both research to identify and optimize Collaboration Compounds as well as pre-clinical development activities leading up to, but will not include, IND-Enabling Studies other than those for which Syros is specifically allocated responsibility pursuant to the Research Plan, which unallocated IND-Enabling Studies will be performed independently from the Research Program by GBT only following the exercise (if any) of the Option. Subject to the immediately following sentence, the Research Plan will also include a reasonably detailed budget for all FTE costs and documented out-of-pocket costs to be incurred by Syros to conduct those activities allocated to it under the

Research Plan (the "**Research Budget**"). As of the Effective Date, the Parties have agreed upon an initial Research Plan, including an initial high-level Research Budget that provides the aggregate annual amounts payable by GBT, covering the first three (3) years of the Research Program, which is attached to this Agreement as **Exhibit A**. Within [***] following the Effective Date, the Parties shall cooperate in good faith to prepare and shall approve an updated Research Budget that sets forth in additional detail the FTE costs and documented out-of-pocket costs to be incurred by Syros to conduct those activities allocated to it under the Research Plan, provided that in no event shall such updated Research Budget exceed the aggregate annual amounts payable by GBT in the initial Research Budget attached to this Agreement as **Exhibit A**. From time to time during the Research Term (and no less frequently than [***]), the JSC shall review the then-current Research Plan and, as appropriate, prepare and approve any needed updates or amendments thereto, subject to the governance and dispute resolution provisions of Section 4.2 and Section 4.3. In addition, no later than [***], the JSC shall prepare a proposed amendment to the Research Plan and Research Budget covering activities for the subsequent calendar year, for review and approval by the JSC subject to the governance and dispute resolution provisions of Section 4.2 and Section 4.3. Once approved by the JSC, each amended Research Plan and Research Budget shall replace the prior Research Plan or Research Budget, as applicable. If the terms of the Research Plan contradict, or create inconsistencies or ambiguities with, the terms of this Agreement, then the terms of this Agreement shall govern.

2.3 Research Term.

(a) **Initial Research Term.** The Research Program shall commence on the Effective Date and end on the earlier of (i) the third (3rd) anniversary of the Effective Date and (ii) the termination of the Research Term pursuant to Section 11.2(a), unless extended as set forth below (the "**Initial Research Term**").

(b) **Extension.** The Initial Research Term may be extended by one or two one-year extensions, in each case by the Parties' written agreement and the Parties' approval of an amended Research Plan (including Research Budget) to include activities to be conducted during such extension (the Initial Research Term together with the period ending on the earlier of (i) the last day of the extension period(s) and (ii) the termination of the Research Term pursuant to Section 11.2(a), collectively, the "**Research Term**"). If either Party desires to extend the then-current Research Term, then no later than [***] before the end of such Research Term, it shall propose to the other Party an updated Research Plan, and if Syros is the proposing Party, it shall include a Research Budget for the extension. If GBT is the proposing Party, and Syros desires to proceed with further consideration of such extension, Syros shall prepare and provide to GBT an updated Research Budget for GBT's consideration.

2.4 Designation of IND Candidates.

(a) From time to time during the Research Term, either Party may nominate to the JSC for consideration as an IND Candidate a particular Collaboration Compound for which the JSC has received a data package meeting the requirements determined by the JSC pursuant to Section 4.1(i). Promptly after any such nomination, each Party shall present to the JSC the data and results of analyses generated by or on behalf of either Party with respect to such Collaboration Compound that are reasonably useful to evaluate such Collaboration Compound as a potential IND

Candidate. GBT solely, acting through its representatives on the JSC or otherwise, shall determine whether any such Collaboration Compound shall be designated as an IND Candidate or whether to propose that additional research activities be conducted with respect to such Collaboration Compound, after which such Collaboration Compound may be reconsidered for nomination as an IND Candidate.

(b) Designation of the first IND Candidate (if any) by GBT under Section 2.4(a) shall trigger commencement of the Option Exercise Period, as set forth in Section 3.1(c), provided that GBT shall be under no obligation to exercise the Option as of such time. If and when GBT exercises the Option, GBT shall initiate IND-Enabling Studies for such Collaboration Compound, and may proceed to IND-Enabling Studies as part of its license rights and obligations under Sections 3.2(a) and 5.2 for any other Collaboration Compound, in each case, at its own expense. For clarity, IND-Enabling Studies and subsequent Development activities conducted by GBT, will not be conducted under the Research Program but will be covered by the exclusive license under Section 3.2(a). Whether or not GBT exercises its Option as of the designation of the first or a later-designated IND Candidate, or at any other point during the Option Exercise Period as provided in Section 3.1(c), the Parties shall nonetheless continue to conduct their activities under the Research Program until the end of the Research Term.

2.5 Research Costs. Each Party shall be solely responsible for all costs such Party incurs to conduct its activities under the Research Plan, except that GBT shall reimburse Syros for the FTE costs and documented out-of-pocket costs incurred by Syros in conducting its activities under the Research Plan, as provided in Section 6.2. Syros shall promptly inform GBT upon Syros' determining that Syros is likely to overspend by more than [***] of its total FTE costs and documented out-of-pocket costs in accordance with the Research Budget for any calendar year. If Syros exceeds its budgeted costs and expenses by more than [***] for such calendar year, it shall provide to GBT an explanation for such overspend. Any overspend of Syros shall be borne by Syros, except to the extent such overspend is less than or equal to [***] of the budgeted costs and expenses for such calendar year, as set forth in the applicable Research Budget (any such amounts, "**Permitted Overspend**").

2.6 Conduct of Research. Each Party shall conduct the activities allocated to it under the Research Plan and Research Budget, and use Commercially Reasonable Efforts to identify at least one IND Candidate. Each Party shall conduct such activities in accordance with the timelines in the Research Plan, in good scientific manner and in compliance with all applicable Laws.

2.7 Research Records. Each Party shall maintain complete, current and accurate records of all activities conducted by it under the Research Program, and all data and other results of analyses resulting from such activities. Such records shall fully and properly reflect all work done and results achieved in the performance of such activities in good scientific manner appropriate for regulatory and patent purposes. Each Party shall document all non-clinical studies in formal written study reports according to applicable Laws and national and international guidelines (e.g., ICH and GLP). Following exercise (if any) of the Option, GBT shall have the right to review and obtain copies of such records maintained by Syros at reasonable times and to obtain access to the original to the extent necessary for regulatory and patent purposes.

2.8 Research Reports. During the Research Term each Party will provide to the JSC, at least [***] a written summary of the research activities conducted and results of analyses generated by or on behalf of such Party or its Affiliates under the Research Program; *provided, however,* that Syros shall not have any obligation to provide to the JSC any Syros Excluded IP. In the event that a Party reasonably requests copies of underlying data or reports generated by or on behalf of the other Party or its Affiliates with respect to particular activities in order for the requesting Party to assess such results, such other Party shall provide such other data or reports. The Parties shall discuss the status, progress and results of the Research Program at JSC meetings. If GBT does not exercise the Option before the end of the Research Term, GBT will provide to the Syros Alliance Manager, within [***] following the later of (a) the Option Effective Date and (b) the expiration of the Option Exercise Period, a written summary of the activities conducted by or on behalf of GBT or its Affiliates in exercising its license to evaluate Collaboration Compounds pursuant to Section 2.1. Notwithstanding anything to the contrary in this Section 2.8, if GBT has not conducted any research activities during any reporting period under this Section 2.8, GBT shall not be required to provide a written summary for such reporting period.

2.9 Materials. To facilitate the conduct of the Research Program or the performance of other activities or the exercise of licenses or other rights under this Agreement, either Party may provide to the other Party certain biological materials or chemical compounds Controlled by the supplying Party for use by the other Party (such materials or compounds, collectively, "**Materials**"). All such Materials shall remain the sole property of the supplying Party, shall be used only in the fulfillment of obligations or exercise of rights under this Agreement and solely under the control of the receiving Party, shall not be used or delivered to or for the benefit of any Third Party without the prior written consent of the supplying Party, shall be returned or destroyed immediately upon the request of the supplying Party, and shall not be used in research or testing involving human subjects. The Materials supplied under this Section 2.9 are supplied "as is" and must be used with prudence and appropriate caution in any experimental work, since not all of their characteristics may be known. For clarity, the Materials do not include any Compound or Product supplied by Syros under a supply agreement entered pursuant to Section 5.6(b).

2.10 Subcontractors. Neither Party shall subcontract any of its obligations under the Research Program without the prior written consent of the other Party, which shall not be unreasonably withheld. As of the Effective Date, GBT has consented to Syros' use of the subcontractors listed on **Exhibit E**. If either Party is bound by confidentiality obligations that would prevent the disclosure to the other Party of any proposed subcontractor, such Party shall use commercially reasonable efforts to obtain any necessary consent to make such disclosure to the other Party, and shall not use any subcontractor hereunder that has not been disclosed and consented to by the other Party. Upon any permitted subcontracting by a Party, such Party shall remain responsible for the work delegated to, and (subject to Section 2.5) payment to, its subcontractors to the same extent it would if it had done such work itself, and shall have or enter into a written agreement with each subcontractor that contains market-appropriate provisions relating to confidentiality and assignment or licensing of resulting intellectual property rights.

ARTICLE 3
OPTION TO LICENSE; LICENSES AND EXCLUSIVITY

3.1 License Option.

(a) **Option Grant**. Subject to Section 3.1(d) and to the terms and conditions hereof, Syros hereby grants to GBT the exclusive option to obtain the grant of the exclusive license rights set forth in Section 3.2 pursuant to the terms and conditions of this Agreement (the "**Option**").

(b) **Option Exercise**. Subject to Section 3.1(d), in order to exercise the Option, GBT must deliver to Syros written notice of its election to exercise the Option during the Option Exercise Period (such timely delivered notice, the "**Option Exercise Notice**"). Upon delivery of the Option Exercise Notice, GBT shall be obligated to pay the Option Exercise Fee pursuant to Section 6.3.

(c) **Option Exercise Period**. GBT may exercise the Option at any time during the period (A) commencing on the earlier of (i) the date of GBT's designation of the first IND Candidate pursuant to Section 2.4, and (ii) if no IND Candidate is so designated as of the end of the Research Term, the date of the expiration or earlier termination of the Research Term, and (B) ending at 11:59 pm Pacific Time on the 180th day after the date of the expiration or earlier termination of the Research Term (the "**Option Exercise Period**").

(d) **Antitrust Filings**.

(i) If GBT desires to exercise the Option, GBT shall reasonably determine in good faith prior to exercise of the Option whether the transactions to be consummated upon the exercise of the Option require any Antitrust Filings. If GBT determines in good faith that any Antitrust Filing(s) is required in connection with GBT's exercise of the Option and GBT desires to exercise the Option, then GBT shall deliver to Syros a notice of intent to exercise such Option within the Option Exercise Period, which notice shall identify any required Antitrust Filings and include GBT's irrevocable binding commitment to complete the exercise of the Option, subject only to satisfaction of the Antitrust Conditions and the terms of this Section 3.1(d) (such notice, a "**Notice of Conditional Exercise**"), whereupon the Option Exercise Period shall be tolled for so long as is necessary for GBT to satisfy applicable Antitrust Conditions, but subject to GBT's compliance with the requirements of Section 3.1(d)(ii) and Section 3.1(d)(iv). For clarity, the Option shall not be deemed exercised and GBT shall not obtain the rights set forth in Section 3.2 unless and until the Parties have obtained satisfaction of any applicable Antitrust Condition for the applicable Antitrust Filing filed pursuant to this Section 3.1(d) and complied with the requirements of this Section 3.1(d).

(ii) If GBT delivers a Notice of Conditional Exercise in accordance with this Section 3.1(d), each of GBT and Syros shall cooperate to prepare and shall make any necessary Antitrust Filings as promptly as is practicable and advisable, with the goal of filing Antitrust Filings within [***] after the date upon which GBT delivers the notice (or such later time as may be agreed to in writing by the Parties) and thereafter each of GBT and Syros shall use commercially reasonable efforts to obtain satisfaction of any applicable Antitrust Condition for any applicable

Antitrust Filing. GBT will be responsible for both Parties' reasonable costs and expenses (including filing fees) associated with any Antitrust Filing, provided that each Party will be responsible for its respective attorneys' fees. Neither Party, or any of its respective Affiliates, will be required to: (A) sell, divest (including through a license), hold separate, transfer or dispose of any assets, operations, rights, product lines, businesses or interests therein (or consent to any of the foregoing actions), or (B) litigate or otherwise formally oppose any determination (whether judicial or administrative in nature) by a Governmental Authority seeking to impose any of the restrictions referenced in clause (A) above.

(iii) Subject to Section 3.1(d)(ii), within [***] after the Parties obtaining satisfaction of any applicable Antitrust Condition for any applicable Antitrust Filing, GBT shall deliver to Syros the Option Exercise Notice and shall be required to make the payment required pursuant to Section 6.3.

(iv) Notwithstanding the foregoing, unless otherwise agreed by the Parties in writing, if satisfaction of any applicable Antitrust Condition has not occurred within [***] after such time as both Parties have made the necessary Antitrust Filings, then, unless mutually agreed to by the Parties in writing, the Option Exercise Period shall automatically be deemed to expire. In such event, Syros shall pay to GBT royalties equal to [***] of any net sales (defined *mutatis mutandis* with the definition of Net Sales in this Agreement) by Syros, its Affiliates or its or their sublicensees of any product containing a Licensed Compound, such royalties not to exceed in the aggregate the amount of research funding paid by GBT to Syros pursuant to Section 2.5. At such time as Syros has paid to GBT royalties on net sales of any such product(s) that total in the aggregate an amount equal to such research funds, Syros' obligations under this Section 3.1(d)(iv) shall terminate.

3.2 License to GBT.

(a) **Licenses**. Subject to the terms and conditions of this Agreement, effective upon the delivery of the Option Exercise Notice and receipt by Syros of the Option Exercise Fee (the "**Option Effective Date**"), Syros hereby grants to GBT an exclusive license, with the right to grant sublicenses as set forth in Section 3.2(c), under the Licensed IP to conduct research with respect to, Develop, make, have made (including manufacture and have manufactured), use, sell, offer for sale, import, export and otherwise exploit and Commercialize Licensed Compounds and Products in the Field in the Territory. Notwithstanding the foregoing, the license granted under this Section 3.2(a) expressly excludes, and nothing in this Agreement shall be interpreted as granting to GBT, any license rights with respect to the Syros Excluded IP.

(b) **Syros Retained Rights**. Syros retains all rights under the Licensed IP except to the extent exclusively licensed to GBT pursuant to Section 3.2(a), including retained rights under the Licensed IP for compounds other than the Licensed Compounds and products other than the Products. Notwithstanding the rights granted to GBT in Section 3.2(a), Syros also retains the right to practice the Licensed IP with respect to Licensed Compounds and Products in the Territory solely as necessary to conduct the activities allocated to Syros under the Research Plan and during the Research Term in accordance with the terms of this Agreement or to supply any Licensed Compound or Product pursuant to any supply agreement entered into pursuant to Section 5.6(b). Nothing in this Agreement shall be interpreted as providing to GBT any right to

conduct de novo research under or to utilize the Syros Platform IP, the Syros Platform or any Syros Platform Improvements.

(c) **Sublicenses**. GBT shall have the right to grant sublicenses through multiple tiers, under any or all of the rights granted in Section 3.2(a), to its Affiliates and to Third Parties. Each sublicense which GBT or its Affiliate or sublicensee grants under any Licensed IP shall be subject to a written agreement that is consistent with the applicable terms and conditions of this Agreement. GBT shall ensure that its sublicensees comply with the applicable terms and conditions of this Agreement, including Article 7 and Article 10 and Section 12.3, which with respect to obligations of GBT thereunder (and the intellectual property definitions used therein) shall apply to each sublicensee *mutatis mutandis* to the same extent as GBT. GBT will remain directly responsible for all of its obligations under this Agreement, regardless of whether any such obligation is delegated to any sublicensees. GBT shall provide Syros with written notice of any sublicense within [***] after it becomes effective (including the identity of the sublicensee and, if applicable, the region in which such rights have been sublicensed) and shall provide Syros with a true and complete copy of each sublicense agreement, subject to GBT's right to redact any confidential or proprietary information contained therein that is not reasonably necessary for Syros to determine compliance with this Agreement. Notwithstanding the foregoing, this Section 3.2(c) (other than the first sentence) shall not apply to the grant by GBT or any sublicensee of a sublicense to any Third Party vendor engaged by GBT or any sublicensee under which such Third Party receives only a non-exclusive limited license under Licensed IP solely to perform activities on behalf of the GBT or such sublicensee, as applicable.

3.3 Transfer of Research Program Know-How in the Licensed IP. Promptly after the Option Effective Date, the Parties shall adopt a transition plan pursuant to which Syros shall, and shall cause any Affiliates to, without additional compensation, disclose and make available to GBT complete and accurate copies of all pre-clinical and non-clinical data, results of analyses thereof and reports with respect to all Licensed Compounds generated by or on behalf of Syros or its Affiliates prior to the Effective Date or during the Research Term prior to the Option Effective Date (other than CMC data, the transfer of which shall be subject to the terms and conditions of Section 5.6(c) and any supply agreement entered into pursuant to Section 5.6(b)). If the Option Effective Date occurs prior to the expiration of the Research Term, on an ongoing basis thereafter, [***], Syros shall make available to GBT complete and accurate copies of all such data, results of analyses and reports generated during the Research Term since the last such transfer under this Section 3.3. Following both the Option Effective Date and the expiration or termination of the Research Term, to the extent Syros identifies any such data, results of analyses and reports that should have been previously delivered in accordance with the foregoing, it shall make available to GBT complete and accurate copies thereof promptly (and in any event within [***]) thereafter. The Parties shall cooperate with each other in good faith to enable a smooth transfer of such data, results of analyses and reports to GBT. Upon GBT's reasonable request and at GBT's reasonable cost and expense, during the [***] period following the later of (a) the end of the Research Term and (b) the Option Effective Date, Syros shall provide reasonable technical consultation, including making appropriate employees available to GBT at reasonable times, places and frequency and upon reasonable prior notice, for the purpose of assisting GBT to understand and use such data, results of analyses and reports in connection with GBT's Development, seeking or obtaining Regulatory Approval for, manufacture or Commercialization of Licensed Compounds and Products. Thereafter during the Term, to the

extent reasonably requested by GBT for GBT's Development of, or seeking or obtaining Regulatory Approval for, manufacture or Commercialization of any Licensed Compound or Product, Syros shall use good faith efforts to respond to any reasonable inquiries from GBT for any data, results of analysis or reports generated by or on behalf of Syros or its Affiliates during the Research Term. Consultation or assistance provided by Syros pursuant to this Section 3.3 shall be at GBT's reasonable cost and expense.

3.4 No Implied Licenses. Except as explicitly set forth in this Agreement, neither Party shall be deemed by estoppel or implication to have granted the other Party any license or other right to any intellectual property of such Party. All rights not otherwise expressly granted hereunder by a Party shall be retained.

3.5 Confirmatory Patent License. Syros shall, if requested to do so by GBT, promptly enter into confirmatory license agreements in the form reasonably agreed by the Parties (and not inconsistent with the terms of this Agreement) for purposes of recording the exclusive licenses granted under this Agreement with such patent offices in the Territory as GBT considers appropriate. Until the execution of any such confirmatory licenses, so far as may be legally possible, Syros and GBT shall have the same rights in respect of the Licensed Patents and be under the same obligations to each other in all respects as if the said confirmatory licenses had been executed.

3.6 Exclusivity.

(a) **Exclusivity Obligations**. Subject to Section 3.6(b) and Section 3.6(c), from the Effective Date until:

(i) the first to occur of (A) the [***] of the Option Effective Date and (B) the date of [***] (the "**Exclusivity Period**"), each Party covenants to the other that it shall not, itself or with or through any Affiliate or Third Party, and shall not grant any Affiliate or Third Party any rights to, clinically develop or commercialize any Competing Compound; or

(ii) the expiration or earlier termination of the Research Term, each Party covenants to the other that it shall not, itself or with or through any Affiliate or Third Party, and shall not grant any Affiliate or Third Party any rights to, knowingly engage in (A) target validation activities for a Collaboration Target to assess the role of such Collaboration Target in fetal hemoglobin up-regulation outside of this Agreement (other than for purposes of confirming compliance with this Section 3.6(a)(ii)) ("**Collaboration Target Validation Activities**") or (B) Drug Discovery and Development Activities with the specific intent to discover or develop any Competing Compound. "**Drug Discovery and Development Activities**" means compound structure discovery and screening, identification of structure-activity relationships or performance of in vitro or in vivo pharmacology, pharmacodynamics or toxicology studies; provided that if in the course of or as a result of any Drug Discovery and Development Activities that are not specifically intended to discover or develop any Competing Compound, a Party or its Affiliate determines that it nonetheless has a compound from such activities that is a Competing Compound, then (i) such compound shall not be considered a Licensed Compound, (ii) such Party and its Affiliates will not conduct any further activities that are prohibited with respect to any Competing

Compound under this Section 3.6(a) (and continued conduct, if any, will be deemed a violation of the preceding clause (B)), except to the extent permitted pursuant to Section 3.6(b).

Notwithstanding the foregoing, each Party's obligations under this Section 3.6(a) shall expire upon the termination of this Agreement in accordance with Section 11.2(e) in the event the Option Exercise Period expires without exercise by GBT of the Option. In addition, for clarity, each Party shall be free (A) to clinically develop and commercialize any Competing Compound at any time after the expiration of the Exclusivity Period during the remainder of the Term (subject in the case of Syros to Section 3.6(c)) and (B) to engage in Collaboration Target Validation Activities, and Drug Discovery and Development Activities with the specific intent to discover or develop any Competing Compound, at any time after the expiration or earlier termination of the Research Term. For clarity, if either Party discovers or preclinically develops a Competing Compound after the expiration or earlier termination of the Research Term but during the remaining Exclusivity Period, such activities alone would not constitute a breach of Section 3.6(a)(i) above or the other provisions of this Section 3.6.

(b) **Exceptions for Competitive Program Transaction**. Notwithstanding Section 3.6(a), subject to clause (v) of this Section 3.6(b), in the event that during the Exclusivity Period a Third Party becomes (x) a controlling (as defined in Section 1.2) Affiliate of a Party as a result of a Change of Control of such Party, or (y) a controlled (as defined in Section 1.2) Affiliate of a Party through a merger, acquisition, reorganization, consolidation or other similar transaction by a Party or any of its Affiliates and, prior to the date on which the agreement(s) effecting such transaction was first executed, such new controlling or controlled Affiliate (or any affiliate of such new controlling or controlled Affiliate) was conducting any Competitive Program (such transaction, a "**Competitive Program Transaction**"):

(i) If such Competitive Program Transaction involves a Change of Control of such Party, then such new Affiliate shall have the right to continue such Competitive Program and such continuation shall not constitute a breach by such Party of its exclusivity obligation set forth in Section 3.6(a), *provided* that (A) such new Affiliate conducts such Competitive Program independently of the activities under this Agreement; (B) such new Affiliate does not use any Licensed IP, Inventions, Program Know-How, Syros Platform IP, Confidential Information of the other Party or Confidential Information of both Parties in the conduct of such Competitive Program; and (C) such Party establishes reasonable internal safeguards designed to ensure that the foregoing requirements are satisfied.

(ii) If such Competitive Program Transaction does not involve a Change of Control of such Party, then such Party shall provide written notice of such Competitive Program Transaction to the other Party within [***] after the effective date thereof, and such Party shall be required to elect, which such election it shall include in any such notice, either to: (A) terminate, or cause such new Affiliate to terminate, such Competitive Program or (B) divest, or cause such new Affiliate to divest, whether by license or otherwise, such Competitive Program.

(iii) If such Party notifies such other Party under Section 3.6(b)(ii) that it intends to terminate, or cause such new Affiliate to terminate, such Competitive Program, then such Party or such new Affiliate shall (A) promptly terminate such Competitive Program as quickly as possible with due regard for patient safety and the requirements of applicable Law; and

(B) confirm to such other Party in writing when such termination has been completed. Such new Affiliate's continuation of any Competitive Program during such period shall not constitute a breach of such Party's obligations under Section 3.6(a); *provided* that (1) such new Affiliate conducts such Competitive Program(s) independently of the activities under this Agreement; (2) such new Affiliate does not use any Licensed IP, Inventions, Program Know-How, Syros Platform IP, Confidential Information of the other Party or Confidential Information of both Parties in the conduct of such Competitive Program; and (3) such Party establishes reasonable internal safeguards designed to ensure that the foregoing requirements are satisfied.

(iv) If such Party notifies such other Party under Section 3.6(b)(ii) that it intends to divest such Competitive Program, then such Party or such new Affiliate shall (A) use commercially reasonable efforts to effect such divestiture as quickly as possible, and in any event within [***] of such Party's notice under Section 3.6(b)(ii); and (B) confirm to such other Party in writing when such divestiture has been completed; *provided, however,* that such [***] period shall be extended for an additional period not to exceed [***] as is necessary to obtain any competition approvals required to complete such divestiture if such Party or such new Affiliate is using commercially reasonable efforts to obtain such approvals. Such Party shall keep such other Party reasonably informed of its efforts and progress in effecting such divestiture until it is completed. If such Party or such new Affiliate effects such divestiture by way of one or more licenses or sublicenses, then the licensor shall be entitled to receive license fees, milestones and royalties on sales of any Competing Compound that constitutes a Competitive Program so divested; *provided* that neither such Party nor such new Affiliate funds or continues to conduct any Competitive Program. Such new Affiliate's continuation of any Competitive Program during such [***] period (and if applicable, additional [***]) period(s) shall not constitute a breach of such Party's obligations under Section 3.6(a); *provided* that (1) such new Affiliate conducts such Competitive Program(s) independently of the activities under this Agreement; (2) such new Affiliate does not use any Licensed IP, Inventions, Program Know-How, Syros Platform IP, Confidential Information of the other Party or Confidential Information of both Parties in the conduct of such Competitive Program; and (3) such Party establishes reasonable internal safeguards designed to ensure that the foregoing requirements are satisfied.

(v) Notwithstanding anything contained in this Section 3.6 to the contrary, (1) in the event that the Competitive Program Transaction occurs after the end of the Research Term, (x) nothing contained in this Section 3.6 shall restrict any new Affiliate of the applicable Party from engaging in any Collaboration Target Validation Activity or any Competitive Drug Discovery Program, (y) such new Affiliate's conduct of any Collaboration Target Validation Activity or any Competitive Drug Discovery Program shall not constitute a breach by such Party of its exclusivity obligation set forth in Section 3.6(a) and (z) such Party and such new Affiliate shall not be required to comply with Section 3.6(b)(i)-(iv) with respect to any Collaboration Target Validation Activity or any Competitive Drug Discovery Program, and (2) in the event that the Competitive Program Transaction occurs prior to the end of the Research Term, any obligations of the applicable Party and any new Affiliate under Section 3.6(b)(i) and 3.6(b)(iv)shall terminate with respect to any Collaboration Target Validation Activity and any Competitive Drug Discovery Program after the end of the Research Term. For clarity, nothing in this Section 3.6(b)(v) shall apply to a Competitive Program that is a program to conduct the clinical development or commercialization of any Competing Compound.

(c) **Consequences of Competing Program or Change of Control**. If (a) Syros or its Affiliate conducts any Competitive Program at any time during the Term, or (b) a Third Party becomes a controlling (as defined in Section 1.2) Affiliate of Syros as a result of a Change of Control of Syros at any time during the Term, then in either case ((a) or (b)) Syros' Co-Detailing Option under Section 5.8 shall immediately terminate and the JDC shall automatically disband in accordance with Section 4.6.

(d) **Covenants Regarding Each Party's IP**.

(i) Notwithstanding any right of GBT to discover or preclinically develop a Competing Product after the Research Term (including during the remainder of the Exclusivity Period), or to conduct research with respect to, develop, make, have made (including manufacture and have manufactured), use, sell, offer for sale, import, export and otherwise exploit and commercialize Competing Products after the Exclusivity Period, GBT covenants to Syros that, during and after the Exclusivity Period, GBT shall not, itself or with or through any Affiliate or Third Party, and shall not grant any Affiliate or Third Party any rights to, use or practice any Licensed IP (other than any Joint IP) or Syros Platform IP in connection with any such activities.

(ii) Notwithstanding any right of Syros to discover or preclinically develop a Competing Product after the Research Term (including during the remainder of the Exclusivity Period), or to conduct research with respect to, develop, make, have made (including manufacture and have manufactured), use, sell, offer for sale, import, export and otherwise exploit and commercialize Competing Products after the Exclusivity Period, Syros covenants to GBT that, during and after the Exclusivity Period, Syros shall not, itself or with or through any Affiliate or Third Party, and shall not grant any Affiliate or Third Party any rights to, use or practice any GBT Licensed IP (other than any Joint IP) in connection with any such activities.

3.7 Syros Covenant Not to Sue. With respect to any Syros Platform IP used, practiced or disclosed to GBT or its Affiliates by Syros or its Affiliates in conducting the Research Program ("**Utilized Syros Platform IP**"), neither Syros nor any of its Affiliates shall institute or prosecute during the Term any legal action against GBT or any of its Affiliates or any sublicensees hereunder to which GBT has granted Development or Commercialization rights with respect to a Licensed Compound or Product and for which Syros has received notice pursuant to Section 3.2(c), alleging that the exploitation by GBT or any of its Affiliates or any such sublicensees of any Licensed Compound or Product in accordance with the terms of this Agreement infringes or misappropriates any such Utilized Syros Platform IP; provided, that Utilized Syros Platform IP shall not include any Syros Platform IP licensed to Syros by [***]. For clarity, nothing contained in this Agreement requires Syros to disclose or transfer to GBT or any of its Affiliates any Syros Platform IP. Unless the Parties otherwise agree in writing, Syros shall not use or practice any [***] in conducting the Research Program.

ARTICLE 4
GOVERNANCE

4.1 Joint Steering Committee. Within [***] following the Effective Date, the Parties shall establish a joint steering committee (the "**Joint Steering Committee**" or the

"**JSC**"), composed of three (3) (or such other number as agreed between the Parties) representatives of each Party having research roles within such Party, each having sufficient experience and responsibility within such Party to make decisions arising within the scope of the JSC's responsibilities. The JSC shall oversee the Research Program and shall in particular:

(a) coordinate the activities of the Parties under the Research Plan and oversee the implementation of the Research Plan;

(b) monitor and receive reports on the progress of the Research Program and review expenditures against the Research Budget;

(c) determine the *in vitro* assay and criteria for characterizing compounds as Collaboration Compounds or Select Related Compounds based on potency and selectivity;

(d) review and select the criteria for efficiently advancing Collaboration Compounds through stages of research under the Research Program;

(e) review and discuss Collaboration Compounds which have been proposed by a Party under Section 2.4(a) as potential IND Candidates to be selected by GBT to advance to IND-Enabling Studies;

(f) subject to Section 4.2, select additional biological targets to be included as Collaboration Targets or de-designate as Collaboration Targets biological targets set forth on Exhibit C;

(g) provide a forum for, and facilitate frequent communications between, the Parties with respect to the Research Program;

(h) prepare, discuss and, subject to Section 4.2, approve any amendments to the Research Plan and/or Research Budget;

(i) determine the requirements for a reasonable and customary candidate selection data package that Syros shall provide to the JSC for the Parties' consideration pursuant to Section 2.4(a); and

(j) perform such other functions as appropriate to further the purposes of the Research Program, as expressly set forth in this Agreement or allocated to the JSC by the Parties in writing.

4.2 Executive Approval. Notwithstanding the foregoing in Section 4.1, (a) the selection by the JSC of additional biological targets to be included as Collaboration Targets or the de-designation as Collaboration Targets by the JSC of biological targets set forth on Exhibit C pursuant to Section 4.1(f) and (b) the approval by the JSC of any amendments to the Research Plan and/or Research Budget pursuant to Section 4.1(h) shall not become effective unless and until approved in writing by an authorized representative of each Party.

4.3 Decision-Making. Except for decisions as to whether a proposed Collaboration Compound should be designated as an IND Candidate, which shall be subject solely to the decision

of GBT, and except as provided in clauses (a) and (b) below, all decisions of the JSC shall be made by unanimous vote, with each Party's representatives collectively having one (1) vote. The Parties will strive to reach consensus on all such decisions of the JSC, acting in good faith and using diligent efforts. If after reasonable discussion and good faith consideration of each Party's view on a particular matter before the JSC that is within its authority, the representatives of the Parties cannot reach unanimous agreement as to such matter within [***] after such matter was brought to the JSC for resolution, such disagreement shall be referred to the Executive Officers (or their designees) of each Party for resolution. If the Executive Officers (or their designees) cannot resolve such matter within [***] after such matter has been referred to them, then:

(a) if such matter concerns the conduct of activities under the Research Program which are consistent with the then current Research Plan and Research Budget, then Syros shall have the final right to decide such matter;

(b) if such matter concerns (i) selection criteria for characterizing compounds as Collaboration Compounds or Select Related Compounds pursuant to Section 4.1(c), or (ii) any proposed increases to the Research Budget that do not entail an increase in FTE resources required to be deployed by Syros, then GBT shall have the final right to decide such matter, and

(c) if such matter concerns any issue not covered by Section 4.3(a) or Section 4.3(b), then the status quo shall prevail with respect to such matter and no changes shall be made except by agreement of the Parties. For clarity, the Parties shall mutually agree on (i) the selection of additional biological targets to be included as Collaboration Targets or the de-designation as Collaboration Targets of biological targets set forth on Exhibit C, (ii) any amendments to the Research Plan, or (iii) any decreases to the Research Budget.

4.4 Termination of the JSC. The JSC shall be disbanded and cease to exist upon the expiration or termination of the Research Term or, if later, the formation of the JDC pursuant to Section 4.5.

4.5 Joint Development Committee. Within [***] following the Option Effective Date, the Parties shall establish a joint development committee (the "**Joint Development Committee**" or the "**JDC**"), composed of three (3) (or such other number as agreed between the Parties) representatives of each Party having clinical, regulatory, or manufacturing development roles within such Party, which shall:

(a) review and discuss GBT's Development plans for IND Candidates and other Collaboration Compounds; and

(b) provide a forum for Syros to provide input, and for GBT to provide updates, to such Development plans.

The JDC shall act solely as an advisory board and communication forum, and not as a decision-making body. For clarity, Syros shall have no authority after the Option Effective Date to make any decisions with respect to the Development, manufacture and Commercialization of Collaboration Compounds or Products in the Field in the Territory (except in relation to the ongoing performance of the Research Plan during the Research Term (as applicable) in accordance with this Agreement).

4.6 Termination of JDC. The JDC shall be disbanded and cease to exist upon the earlier of: (a) the first approval of an MAA by the applicable Regulatory Authority for the first Product; (b) Syros' uncured material breach of its exclusivity obligations under Section 3.6; (c) GBT's termination of the Research Program pursuant to Section 11.2(a); (d) a Change of Control of Syros; or (e) any conduct by Syros or its Affiliates of any Competitive Program Transaction.

4.7 Committee Membership and Meetings.

(a) **Members.** Each Party may replace its representatives on any Committee on written notice to the other Party. Each Party shall appoint one (1) of its representatives on each Committee to act as a co-chairperson of such Committee. The co-chairpersons of each Committee will be responsible for sending invitations and agendas for Committee meetings to all members at least [***] before the next scheduled meeting and shall jointly prepare and circulate reasonably detailed minutes of each Committee meeting, but will otherwise have no additional powers or rights beyond those held by other Committee representatives.

(b) **Meetings**. Each Committee shall hold meetings at such times as it elects to do so or as either Party reasonably requests, but in no event shall such meetings be held less frequently than [***] for the JSC and [***] for the JDC. Meetings may be held in person or by audio or video teleconference. In-person meetings shall be held at locations agreed by the Parties. Each Party shall be responsible for all of its own expenses of participating in Committee meetings. No action taken at any meeting of any Committee shall be effective unless at least one representative of each Party is participating.

(c) **Non-Member Attendance**. Each Party may from time to time invite a reasonable number of participants, in addition to its representatives, to attend the Committee meetings in a non-voting capacity; provided that (i) such participants shall be bound by confidentiality and non-use obligations consistent with the terms of this Agreement and no less stringent than the confidentiality and non-use obligations contained herein, and (ii) each Party shall provide prior written notice to the other Party if it has invited any Third Party (including any consultant) to attend such a meeting.

4.8 Limitations of Committee Authority. Each Committee shall have only the powers expressly assigned in this Article 4 and in Article 2, and shall not have the authority to: (a) modify or amend the terms and conditions of this Agreement; (b) waive or determine either Party's compliance with the terms and conditions of this Agreement; or (c) decide any issue in a manner that would conflict with the express terms and conditions of this Agreement.

4.9 Alliance Managers. In addition to the JSC described in Section 4.1, GBT and Syros each acknowledge and agree that it would be beneficial to the Research Program for each to have a senior representative with a general understanding of the activities under such programs to act as an alliance manager during the Research Term (each, an "**Alliance Manager**"), and each will appoint such person to the extent each Party in its sole discretion determines it is practical. It is envisioned that the Alliance Managers will serve as a single point of contact within each Party with responsibility for facilitating communication and collaboration between the Parties. Each Party's Alliance Manager may attend JSC and JDC meetings as appropriate and will facilitate dispute resolution and decision-making process within the JSC in accordance with the terms of

this Agreement, provided that the Alliance Managers shall not have final decision-making authority with respect to any matter under this Agreement.

ARTICLE 5
DEVELOPMENT AND COMMERCIALIZATION

5.1 General. As between the Parties, from and after the Option Effective Date, GBT shall be solely responsible, at its own expense, for all aspects of the Development (including IND-Enabling Studies other than those for which Syros is specifically allocated responsibility pursuant to the Research Plan), manufacture and Commercialization of Licensed Compounds and Products in the Field in the Territory pursuant to this Agreement.

5.2 Diligence. During the Term, GBT shall use Commercially Reasonable Efforts to Develop (including to seek and obtain Regulatory Approval of) and, if Regulatory Approval is obtained, Commercialize at least one Product in the Field in the United States and in the Major Markets.

5.3 Development Records. GBT shall maintain complete, current and accurate records of all Development activities it conducts under this Agreement and all data and other information resulting from such activities. Such records shall fully and properly reflect all work done and results achieved in the performance of the Development activities in good scientific manner appropriate for regulatory and patent purposes. GBT shall document all non-clinical studies and clinical trials in formal written study reports according to applicable Laws and national and international guidelines (*e.g.*, ICH, good clinical practices, GLP, and GMP).

5.4 Subcontractors. GBT may perform its Development and Commercialization activities through one or more Third Party subcontractors. GBT shall remain responsible for the work delegated to, and payment to, such subcontractors to the same extent it would if it had done such work itself, and shall have entered into a written agreement with each such subcontractor that contains market-appropriate provisions relating to confidentiality and assignment or licensing of resulting intellectual property rights.

5.5 Regulatory Activities.

(a) **Regulatory Materials and Approvals**. GBT shall be responsible for preparing and filing all Regulatory Materials and seeking all Regulatory Approvals in the Field in the Territory, including preparing all reports necessary as part of a Marketing Authorization Application. As between the Parties, all Regulatory Materials for any Product in the Territory shall be filed in the name of GBT, and GBT alone shall be responsible for all communications and other dealings with any Regulatory Authority relating to any Product in the Territory. As between the Parties, subject to Section 11.3, GBT shall be the legal and beneficial owner of all Regulatory Approvals in the Territory.

(b) **Recalls, Suspensions or Withdrawals**. As between the Parties, subject to the applicable recall provisions of any supply agreement entered into by the Parties pursuant to Section 5.6, GBT shall be solely responsible for handling any recall, market suspension or market withdrawal in the Field in the Territory at its sole cost and expense. If a recall, market suspension or market withdrawal is mandated by a Regulatory Authority in the Territory, as between the

Parties, GBT shall initiate such a recall, market suspension or market withdrawal in compliance with applicable Law.

(c) **Global Safety Database.** GBT shall establish, hold and maintain (at GBT's sole cost and expense) the global safety database for each Product Developed or Commercialized in the Territory.

5.6 Manufacturing.

(a) **Responsibility**. Following the expiration of the Research Term, GBT shall be solely responsible, at its sole expense, for all manufacture of Licensed Compounds and Products for use under this Agreement, except as may be expressly set forth herein or agreed by the Parties in writing.

(b) **Potential Supply by Syros**. Within [***] following the Option Effective Date (or such other time upon mutual agreement by the Parties), GBT may, upon written notice, request that Syros manufacture and supply to GBT its reasonable requirements for Collaboration Compounds or Products for any IND Candidate for the conduct of IND-Enabling Studies or First-in-Human Clinical Trials. In the event of any such notice, the Parties shall negotiate in good faith to enter into a mutually acceptable and commercially reasonable supply agreement and associated quality agreement, under which GBT shall purchase such Licensed Compound or Product at a price equal to Syros's internal costs (at the FTE Rate) and out-of-pocket costs to manufacture such Licensed Compound or Product. In connection with such negotiation, Syros shall confer with GBT regarding any Third Party manufacturer that Syros intends to use to carry out such activities, including the technology transfer provisions included or proposed to be included in such agreement. In the event GBT is not satisfied with the selection of such Third Party manufacturer or such technology transfer provisions and notifies Syros thereof in writing within [***] of disclosure by Syros thereof, neither GBT nor Syros shall have any obligation to negotiate a supply agreement (and Syros shall have no obligation to supply hereunder) unless otherwise agreed in writing.

(c) **Manufacturing Technology Transfer.** Following the Option Effective Date and at a time reasonably requested by GBT, the Parties shall cooperate to facilitate a transfer of the relevant manufacturing process for the applicable Licensed Compound or Product to GBT or its designee. Syros shall exercise its rights under the terms of the applicable upstream manufacturing agreement between Syros and the Third Party manufacturer to require the Third Party manufacturer to conduct such transfer pursuant to the terms and conditions of the applicable agreement, which agreement shall entitle Syros to receive or direct a technology transfer consistent with the Third Party manufacturer's customary transfer standard operating procedure or as otherwise provided in the applicable agreement. Syros shall provide reasonable assistance to GBT in connection with such manufacturing transfer by making Syros' technical personnel who are knowledgeable about the manufacturing process reasonably available to GBT for consultation and, if applicable, introducing GBT to Syros's Third Party manufacturer(s) for Licensed Compounds and Products. GBT shall reimburse all reasonable and documented internal costs (at the FTE Rate) and reasonable and documented out-of-pocket costs incurred by Syros to conduct and assist GBT with such technology transfer.

5.7 Reports. On a [***], during the period commencing on the termination of the JDC and ending on the earlier of (a) [***] and (b) [***], GBT shall provide Syros with a summary of GBT's material Development activities with respect to each Product in the Territory since the last such report that is sufficiently detailed for Syros to confirm GBT's compliance with its obligations pursuant to this Article 5 and progress towards the achievement of the milestone events set forth in Section 6.4(a). On a [***] basis during the Term, GBT shall (1) provide to Syros a list of all Collaboration Compounds and Select Related Compounds determined by or on behalf of GBT or its Affilates during the applicable [***] period to meet the *in vitro* assay criteria for characterizing compounds as Collaboration Compounds or Selected Related Compounds determined by the JSC pursuant to Section 4.1(c) and (2) notify Syros of each commencement of IND Enabling Studies with respect to any Licensed Compound or Product.

5.8 Co-Detailing Option.

(a) **Grant of Co-Detailing Option**. Subject to potential termination as provided in Section 3.6(c), and the payment to GBT of the Co-Detailing Option Exercise Fee pursuant to Section 5.8(b), GBT hereby grants Syros a one-time option to provide [***] of the details for the first Product (other than Combination Products) for which the filing of an NDA has been accepted by the FDA (the "**Co-Detail Product**") in the United States, as further described in this Section 5.8 (the "**Co-Detailing Option**"). Notwithstanding the foregoing, if Syros does not exercise the Co-Detailing Option with respect to the first such Product for which the filing of an NDA has been accepted by the FDA, then the Co-Detailing Option shall not apply to any future Products and this Section 5.8 shall become null and void. Notwithstanding the foregoing, (i) the Co-Detailing Option (if not then exercised or expired) will terminate immediately upon a Change of Control of Syros, (ii) if Syros exercises its Co-Detailing Option and subsequently undergoes a Change of Control, Syros shall not have the right to assign its rights to co-detail under this Section 5.8 in connection with such Change of Control, unless GBT consents to such assignment in GBT's sole discretion, and (iii) GBT shall have the right, upon [***] written notice, where the Co-Detailing Option has as of such time been exercised by Syros, to terminate Syros's rights to co-detail under this Section 5.8 in the event that Syros or its Affiliate clinically develops or commercializes any Competing Product, or in the event of an assignment of this Agreement in its entirety by Syros (other than an assignment to an Affiliate of Syros), in any case unless GBT otherwise consents to the continuation of such co-detail rights in such circumstances, which consent may be withheld in GBT's sole discretion.

(b) **Co-Detailing Option Exercise**. Syros may, in its sole discretion, exercise the Co-Detailing Option by (i) providing written notice to GBT at any time within [***] following delivery of written notice to Syros of the FDA's acceptance of a filing of an NDA for the Co-Detail Product (the "**Exercise Notice**") and (ii) paying to GBT the Co-Detailing Option Exercise Fee within [***] of execution by the Parties of the Co-Detailing Agreement in accordance with Section 5.8(c). For clarity, if Syros does not provide the Exercise Notice or pay the Co-Detailing Option Exercise Fee to GBT within the respective periods set forth in the preceding sentence, then the Co-Detailing Option and the Co-Detailing Agreement shall immediately and automatically terminate.

(c) **Co-Detailing Agreement**. Within [***] following Syros' exercise of the Co-Detailing Option, the Parties shall negotiate in good faith and enter into a co-detailing agreement (the "**Co-Detailing Agreement**") setting forth the terms and conditions of Syros's co-detailing of the Co-Detail Product. The Co-Detailing Agreement shall be consistent with this Section 5.8 and shall contain additional mutually agreed reasonable and customary terms.

(d) **Co-Detailing Key Terms**.

(i) If Syros timely exercises the Co-Detailing Option in accordance with Section 5.8(b), Syros' right to co-detail the Co-Detail Product shall commence [***] after the First Commercial Sale of the Co-Detail Product in the United States (the "**Co-Detail Start Date**"). Syros's right to co-detail the Co-Detail Product in the United States shall terminate on the [***] anniversary of the Co-Detail Start Date, and thereafter Syros shall have no right to conduct any detailing of the Co-Detail Product.

(ii) GBT shall reimburse Syros for Syros' detailing efforts on a [***], as mutually agreed upon and further described in the Co-Detailing Agreement.

(e) **Decision-Making**. Notwithstanding the Co-Detailing Option exercise by Syros under this Section 5.8, GBT shall maintain full responsibility and decision-making authority with respect to the Commercialization of the Co-Detail Product, including sales force sizing, determination and methodology for determining, the requisite number of details in any given year, target call lists, and the like.

ARTICLE 6

FINANCIAL PROVISIONS

6.1 Upfront Payment. GBT shall pay to Syros a one-time, non-refundable, non-creditable upfront payment of Twenty Million Dollars ($20,000,000) within fifteen (15) Business Days after the Effective Date.

6.2 Reimbursement of Research Costs. Within [***] after the end of each calendar quarter during which Syros has incurred any FTE-related costs (calculated by multiplying the applicable number of FTEs by the FTE Rate) or documented out-of-pocket costs to conduct the Research Program in accordance with the Research Plan (including the Research Budget set forth therein) (the "**Incurred Budgeted Costs**"), Syros shall submit to GBT a reasonably detailed report setting forth all such Incurred Budgeted Costs and all Permitted Overspend incurred in such calendar quarter (the "**Approved Costs**") as well as any other FTE-related costs (calculated by multiplying the applicable number of FTEs by the FTE Rate) or documented out-of-pocket costs to conduct the Research Program in accordance with the Research Plan (but, for clarity, beyond the Research Budget) incurred in such calendar quarter (the "**Unapproved Costs**"). Such report shall be accompanied by an invoice for all Approved Costs. Upon GBT's request, Syros shall promptly provide GBT with reasonable supporting documentation, including with respect to any Unapproved Costs, and use good faith efforts to resolve any dispute or inquiry that GBT may have over any amount so invoiced. GBT shall pay to Syros an amount equal to the Approved Costs so

invoiced within [***] after the receipt of each such invoice. At GBT's sole discretion, it may also pay to Syros some or all of the Unapproved Costs, but shall not be required to do so.

6.3 Option Exercise Fee. Upon delivery of the Option Exercise Notice, GBT shall pay to Syros a non-refundable, non-creditable exercise fee equal to [***] ($[***]) (the "**Option Exercise Fee**") within [***] after delivery of such notice.

6.4 Clinical and Commercial Milestone Payments.

(a) **Milestone Events.** Subject to the remainder of this Section 6.4, on a Licensed Compound-by-Licensed Compound basis, GBT shall pay to Syros the non-refundable, non-creditable clinical and commercial milestone payments set forth in the table below upon the achievement of the corresponding milestone event set forth in the table below for each of the first two (2) Indications for the first Product containing such Licensed Compound to achieve such milestone event with respect to such Indication, provided that milestone event number 1 below shall only be payable with respect to the first (1st) Indication for which such milestone is achieved for such Licensed Compound. For clarity, (i) for the purposes of this Section 6.4 and Sections 6.5 and 6.6, Products will be considered different Products only if they contain different Licensed Compounds and (ii) the same milestone event may be achieved with respect to the first and second Indications in a single clinical trial (e.g., in the case of a first Initiation of a First-In-Patient Clinical Trial for which the clinical trial protocol covers more than one Indication). GBT shall notify Syros within [***] after the achievement of each milestone event below. After achievement, Syros may issue an invoice for the applicable milestone payment, and GBT shall pay such invoice within [***] after receipt thereof.

Milestone Event	**Milestone Payment – First Indication**	**Milestone Payment – Second Indication**
1. [***]	$ [***]	$ [***]
2. [***]	$ [***]	$ [***]
3. [***]	$ [***]	$ [***]
4. [***]	$ [***]	$ [***]
5. [***]	$ [***]	$ [***]
6. [***]	$ [***]	$ [***]

7. [***]	$[***]	$[***]
Total (per Licensed Compound)	$[***]	$[***]

(b) **Milestones for Backup Compounds.** Notwithstanding anything to the contrary in Section 6.4(a), with respect to a Product for an Indication that achieves a milestone event pursuant to Section 6.4(a), if GBT terminates the Development or Commercialization of the Licensed Compound contained in such Product in favor of a replacement Licensed Compound directed to the same therapeutic target (such replacement, a "**Backup Compound**"), then such Backup Compound shall be deemed the same as the Licensed Compound for the purposes of determining milestone payments owed under Section 6.4(a), and GBT shall not pay any milestone payment for the achievement of a milestone event for an Indication for a Product containing such Backup Compound if GBT has already made a milestone payment for the achievement of such milestone event for such Indication for a Product containing such Licensed Compound.

(c) **Catch-Up Payments**. If milestone event #[***] is achieved for a Licensed Compound and Indication, and at such time any earlier milestone event (i.e., milestone event #[***], as applicable) has not been achieved for such Licensed Compound and Indication, then such earlier milestone event will be deemed achieved and the corresponding milestone payment will be due. If milestone event #[***] is achieved for a Licensed Compound and Indication, and at such time any of milestone event #[***] has not been achieved for such Licensed Compound and Indication, then such earlier milestone event will be deemed achieved and the corresponding milestone payment will be due. If milestone event #[***] is achieved for a Licensed Compound and Indication, and at such time any of milestone event #[***] has not been achieved for such Licensed Compound and Indication, then such earlier milestone event will be deemed achieved and the corresponding milestone payment will be due. If milestone event #[***] is achieved for a Licensed Compound and Indication, and at such time any of milestone event #[***] has not been achieved for such Licensed Compound and Indication, then such earlier milestone event will be deemed achieved and the corresponding milestone payment will be due.

6.5 Sales Milestones.

(a) **Sales Milestone Events**. On a Licensed Compound-by-Licensed Compound basis, GBT shall pay to Syros the one-time (per Licensed Compound) non-refundable, non-creditable sales milestone payments set forth in the table below when the aggregate annual Net Sales of all Products containing such Licensed Compound for any and all uses in the Field sold in the Territory in a calendar year first reach the corresponding threshold value indicated below.

Milestone Event	Milestone Payment
1. First calendar year in which aggregate annual Net Sales of Products exceed $[***]	$ [***]
2. First calendar year in which aggregate annual Net Sales of Products exceed $[***]	$ [***]
3. First calendar year in which aggregate annual Net Sales of Products exceed $[***]	$ [***]
4. First calendar year in which aggregate annual Net Sales of Products exceed $[***]	$ [***]
Total (for each Licensed Compound)	$ [***]

(b) **Notice and Payment.** As part of the royalty report required by Section 6.6(f), GBT shall provide written notice to Syros if the aggregate annual Net Sales in respect of a Product in the Territory first reach any threshold value set forth in Section 6.5(a) above during the time period to which such report pertains. After the receipt of such notice from GBT, Syros shall submit to GBT an invoice for the corresponding sales milestone payment. GBT shall pay such amount to Syros within [***] after the receipt of such invoice.

6.6 Royalty Payments.

(a) **Royalty Rate.** On a Product-by-Product basis, GBT shall make quarterly royalty payments to Syros on the aggregate Net Sales of such Product achieved in the applicable calendar year, as calculated by multiplying the applicable royalty rate(s) set forth in the table below by the corresponding amount of incremental, aggregated Net Sales of such Product for any and all uses in the Field in the Territory achieved in the applicable calendar year.

Aggregate Net Sales of Each Product in the Territory in a Calendar Year	Royalty Rate
On that portion of aggregate Net Sales of such Product less than or equal to $[***] in a calendar year	[***]%
On that portion of aggregate Net Sales of such Product greater than $[***] but less than or equal to $[***] in a calendar year	[***]%
On that portion of aggregate Net Sales of such Product greater than $[***] but less than or equal to $[***] in a calendar year	[***]%
On that portion of aggregate Net Sales of such Product greater than $[***] in a calendar year	[***]%

(b) **Royalty Term.** GBT's obligation to pay royalties pursuant to this Section 6.6 shall expire, on a Product-by-Product and country-by-country basis, upon the expiration of the Royalty Term for such Product in such country.

(c) **Royalty Conditions.** The royalty payments under this Section 6.6 shall be subject to the following conditions:

(i) Only one (1) royalty shall be due with respect to each unit of Product, without regard to whether there is more than one Valid Claim or Patent Right covering such Product.

(ii) For the purpose of determining the applicable royalty tiers, the annual Net Sales of each Product in the Territory shall be aggregated separately. In addition, the Net Sales of a Product sold in a country after the expiration of the Royalty Term for such Product in such country shall not be included in the calculation of annual Net Sales to determine the applicable royalty tiers.

(d) **Royalty Reductions**. If, during any portion of the Royalty Term for a Product and country, there is no Licensed Covering Claim for such Product (or the applicable Licensed Compound) in such country, then the royalties payable under Section 6.6(a) on Net Sales of such Product in such country in respect of such portion of such Royalty Term will be reduced:

(i) by subtracting [***] (i.e., [***]%) from the rates listed in Section 6.6(a) (e.g., reducing a royalty rate from [***]% to [***]%) for any portion of such Royalty Term for which there is both (A) a Covering Claim in an Other Royalty Patent and (B) unexpired Regulatory Exclusivity, in each case (A) and (B) for such Product in such country;

(ii) by subtracting [***] (i.e., [***]%) from the rates listed in Section 6.6(a) (e.g., reducing a royalty rate from [***]% to [***]%) for any portion of such Royalty Term for which there is no Covering Claim for such Product in such country but there is unexpired Regulatory Exclusivity for such Product in such country; or

(iii) to [***] ([***]%) of the rates listed in Section 6.6(a) for any portion of such Royalty Term for which there is no Regulatory Exclusivity for such Product in such country.

(e) **Royalty Floor.** In no event shall the amounts payable to Syros under this Section 6.6 in respect of a calendar quarter be reduced by operation of Sections 6.6(d) and 7.9 by more than [***]% of what would otherwise be due in respect of such calendar quarter by operation of this Section 6.6 without regard to Sections 6.6(d) and 7.9.

(f) **Royalty Reports and Payment.** Within [***] after the end of each calendar quarter (but with respect to the fourth (4th) calendar quarter of any calendar year, within [***] after the end of such calendar year), commencing with the calendar quarter during which the First Commercial Sale of the first Product is made anywhere in the Territory, GBT shall provide Syros with a statement, on a Product-by-Product basis, of the amount of Net Sales of each Product stated in GBT's "sales" line of its audited financial statements, including, solely if such amounts are not reported on a Product-by-Product basis, the gross

invoiced amount and the itemized deductions taken to arrive at Net Sales, during the applicable calendar quarter, the applicable exchange rates, and a calculation of the amount of royalty payment due on such Net Sales for such calendar quarter, including any royalty reductions and deductions under Sections 6.6(d) and 7.9 and any Combination Product allocations. No later than [***] after the delivery of each such royalty statement (and in any event within [***] after the end of each calendar year and [***] after the end of each of the first three (3) calendar quarters of any calendar year), GBT shall pay Syros in Dollars all royalties owed with respect to Net Sales for such calendar quarter.

6.7 Third Party Payment Obligations.

(a) Subject to Section 7.9, GBT shall be responsible for the payment of royalty, milestone and other payments due to Third Parties under any agreements between such Party (or its Affiliates) and Third Parties on account of GBT's and its Affiliates' and sublicensees' Development, manufacture and Commercialization of Products in the Field in the Territory. GBT shall not be responsible for the payment of royalty, milestone and other payments due to Third Parties under any license agreements between Syros (or its Affiliates) and any Third Parties.

6.8 Currency; Exchange Rate; No Refunds or Credits; Interest.

(a) **Currency.** All payments to be made by a Party to the other Party under this Agreement shall be made in Dollars by bank wire transfer in immediately available funds to a bank account designated by written notice from the Party receiving the payment.

(b) **Exchange Rate.** The rate of exchange to be used in computing the amount of currency equivalent in Dollars for any Net Sales of Product shall be the rate used by GBT in its financial reporting in accordance with GAAP or IFRS. For any other amount that is to be paid by one Party to the other Party and that is expressed in a foreign currency, the paying Party shall convert such amount into Dollar equivalents using the arithmetic average of the exchange rates for the purchase of Dollars as published in *The Wall Street Journal*, Eastern Edition, for the calendar quarter to which such payment relates.

(c) **Interest.** Each Party shall be liable for interest on the aggregate amount of any payments that are not paid on or before the date such payments are due under this Agreement at a rate per annum equal to the lesser of the three (3) month LIBOR rate for Dollars as reported in the *Wall Street Journal*, Eastern Edition, for the applicable period (or in the event that the LIBOR is no longer an applicable reference rate, such reasonably equivalent alternative as the Parties reasonably agree), plus [***] ([***]%), calculated based on the number of days such payments are paid after the date such payments are due, or if lower, the highest rate allowed by applicable Law, commencing on the date such payments are due and ending when paid; provided that with respect to any disputed payments, no interest payment shall be due until such dispute is resolved and the interest which shall be payable thereon shall be based on the finally-resolved amount of such payment, calculated from the original date on which the disputed payment was due through the date on which payment is actually made.

6.9 Taxes.

(a) **Taxes on Income.** Each Party shall be solely responsible for the payment of all taxes imposed on its share of income arising directly or indirectly from the activities of the Parties under this Agreement.

(b) **Tax Cooperation.** The Parties agree to cooperate with one another and use reasonable efforts to reduce or eliminate tax withholding or similar obligations in respect of royalties, milestone payments and other payments made under this Agreement. To the extent a Party is required to deduct and withhold taxes on any payment to the other Party, such Party shall deduct the amounts of such taxes from the payment, pay such amounts to the proper Governmental Authority in a timely manner and promptly transmit to the other Party an official tax certificate or other evidence of such withholding sufficient to enable the other Party to claim such payment of taxes. The Party receiving the payment shall provide the Party making the payment any tax forms that may be reasonably necessary in order for the Party making the payment not to withhold tax or to withhold tax at a reduced rate under an applicable bilateral income tax treaty. Each Party shall provide the other with reasonable assistance to enable the recovery, as permitted by applicable Laws, of withholding taxes, value added taxes, or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the Party bearing such withholding tax or value added tax. Notwithstanding the foregoing, if the Party making the payment takes any actions that would increase any required withholding taxes that otherwise would not be required absent such action, including a change in tax residence, (sub)license or assignment of this Agreement or any rights or obligations hereunder by law or otherwise, or any merger, acquisition, asset purchase or sale of all or substantially all of its business or assets, the Party making the payment shall increase the amount so payable as necessary so that after such deduction or withholding of withholding taxes has been made, the other Party receives the amount it would have received had no such deduction or withholding been made.

6.10 Financial Records and Audit.

(a) Each Party shall maintain complete and accurate records in sufficient detail to permit the other Party to confirm the accuracy of Approved Costs, Net Sales, royalty payments and other amounts payable under this Agreement and to verify the achievement of all sales milestone events under this Agreement. Upon [***] prior notice, such records shall be open during regular business hours for a period of [***] from the creation of individual records for examination at the auditing Party's expense, and not more often than [***], by an independent certified public accountant selected by the auditing Party and reasonably acceptable to the audited Party for the sole purpose of verifying for the auditing Party the accuracy of the financial reports furnished by the audited Party pursuant to this Agreement or of any payments made, or required to be made, under this Agreement. Any such auditor shall not disclose the audited Party's confidential information to the auditing Party, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by the audited Party or the amount of payments under this Agreement. Records for a particular time period may not be audited more than [***].

(b) Any amounts shown to be owed but unpaid, or overpaid and in need of reimbursement, shall be paid or refunded (as the case may be) within [***] after the

accountant's report. If the audited Party is the Party that is required to make such additional payment or refund, the audited Party shall also pay interest as provided in Section 6.8(c) on such underpayment or overcharge by the audited Party from the original due date(s).

(c) The auditing Party shall bear the cost of such audit unless such audit reveals an underpayment or overcharge by the audited Party that resulted from a discrepancy in a financial report provided by the audited Party hereunder, which underpayment or overcharge was more than [***] ([***]%) of the amount actually due for the audited time period, in which case the audited Party shall reimburse the auditing Party for the reasonable out-of-pocket costs for such audit.

ARTICLE 7
INTELLECTUAL PROPERTY RIGHTS

7.1 Inventorship and Ownership

(a) **Inventorship**. Inventorship of Inventions conceived or reduced to practice under the Research Program or thereafter during the Term shall be determined in accordance with the patent Laws of the United States.

(b) **Ownership**. Syros shall solely own any Syros Sole Inventions, Syros Sole Patents, Syros Sole Know-How and Syros Platform IP. GBT shall solely own any GBT Sole Inventions, GBT Sole Patents or GBT Sole Know-How. The Parties shall jointly own any Joint IP. Except to the extent either Party is restricted by the licenses granted to the other Party or exclusivity obligations under this Agreement, each Party shall be entitled to practice, license, assign and otherwise exploit the Joint IP without the duty of accounting or seeking consent from the other Party (and any such required consent is hereby deemed granted).

(c) **Disclosure.** Each Party shall promptly disclose to the other Party all Inventions conceived by such Party, including all invention disclosures or other similar documents submitted to such Party by its or its Affiliates' employees, agents or independent contractors relating to such Inventions, and shall also respond promptly to reasonable requests from the other Party for additional information relating to such Inventions.

(d) **Assignment.** Each Party shall, and does hereby, assign, and shall cause its Affiliates and its and their (sub) licensees to so assign, to the other Party, without additional compensation, such right, title and interest in, to and under the Joint Program IP as is necessary to fully effect ownership as provided for in Section 7.1(b). GBT shall, and does hereby, assign, and shall cause its Affiliates to assign, to Syros, without additional compensation (but at Syros' sole and reasonable expense, except in the case of GBT material breach), its and their entire right, title and interest in, to and under any Inventions and Know-How that constitute Syros Platform Improvements, and any Patent Rights that cover or claim Syros Platform Improvements. Notwithstanding the foregoing, GBT shall only be required to transfer to Syros tangible embodiments of Inventions or Know-How that constitute Syros Platform Improvements.

(e) **Personnel Obligations.** To the extent permitted by applicable Law, each employee or agent of a Party or its respective Affiliates performing work under this Agreement shall, prior to commencing such work, be bound by invention assignment obligations, including: (i) promptly reporting any invention, discovery, process or other intellectual property right; (ii)

presently assigning to the applicable Party or Affiliate all of his or her right, title and interest in and to any invention, discovery, process or other intellectual property; (iii) reasonably cooperating in the preparation, filing, prosecution, maintenance and enforcement of any patent or patent application; and (iv) performing all acts and signing, executing, acknowledging and delivering any and all documents required for effecting the obligations and purposes of this Agreement. It is understood and agreed that such invention assignment agreement need not reference or be specific to this Agreement. Each independent contractor of a Party or its respective Affiliates performing work under this Agreement shall, prior to commencing such work, be bound by commercially reasonable invention assignment or grantback obligations.

(f) **Unaided Memory**. Notwithstanding either Party's assignment or exclusive license to the other Party of any information pursuant to Section 3.2(a), Section 7.1(d), Section 7.4 or Section 11.3(b)(i), the Parties acknowledge the practical difficulty of policing the use of information in the unaided memory of a Party or its Affiliates and its and their officers, directors or employees, and as such each Party agrees that neither Party or its Affiliates shall be liable for the use by any of such Party or its Affiliates' officers, directors or employees of specific information assigned or exclusively licensed to the other Party pursuant to Section 3.2(a), Section 7.1(d), Section 7.4 or Section 11.3(b)(i), as applicable, that is retained in the unaided memory of such officer, director or employee; provided that (a) such officer, director or employee is not aware that such information is owned or controlled by, or the Confidential Information of, the other Party, as applicable, at the time of such use; and (b) the foregoing is not intended to grant, and shall not be deemed to grant, such Party, its Affiliates, or its officers, directors and employees (i) a right to disclose any such information that is such other Party's Confidential Information, or (ii) a license under any Patents, Know-How or other intellectual property rights of such other Party.

7.2 Patent Prosecution. For the purpose of this Section 7.2 and Section 7.3, "**prosecution**" or "**prosecute**" shall mean, with respect to any Patent Rights, the preparation, filing, prosecution (including conducting all correspondence and interactions with any patent office and seeking, conducting and defending any interference, inter parties review proceeding, reissue proceeding, reexamination, post grant review proceeding, patent interference proceeding, opposition proceeding and any appeals therefrom) and maintenance (including payment of any patent annuity or maintenance fees) of such Patent Rights, as well as any requests for patent term adjustments, patent term extensions, supplementary protection certificates, or their equivalents with respect to such Patent Rights. This Section 7.2 and Section 7.3 contemplate the transfer or other modification of the Parties' respective obligations with respect to certain Patent Rights based on the applicable Transfer Dates, and for such purpose, "**Transfer Date**" shall mean, on a patent application-by-patent application basis (a) with respect to each Syros Sole Patent or Joint Patent, (i) if as of the Option Effective Date Syros has filed a PCT application with respect to such Patent Right, the Option Effective Date, (ii) if as of the Option Effective Date Syros has filed a provisional application with respect to such Patent Right and has not filed a PCT application with respect to such Patent Right, the date on which Syros files a PCT application with respect to such Patent Right and (iii) if as of the Option Effective Date Syros has not filed any provisional or PCT application with respect to such Patent Right, the Option Effective Date and (b) with respect to each GBT Sole Patent that is not an Other Royalty Patent, the Option Effective Date. All references to "PCT application" in this Section 7.2 shall be deemed to include any non-provisional patent application filed in the United States, and for purposes of the Transfer Date provisions above, shall refer to the earlier of the filing of the PCT application or the filing of the non-

provisional patent application in the United States. After each Transfer Date, the Parties shall reasonably cooperate to effect an orderly transition of each Party's prosecution responsibilities under this Section 7.2.

(a) **Syros Platform Patents and Other Syros Patents.** Syros shall continue to own, and, as between the Parties, shall have the sole right, but not the obligation, to prosecute with the appropriate patent authorities in the Territory any Syros Platform Patents and any Other Syros Patents.

(b) **GBT Licensed IP.** GBT shall continue to own, and (except in the case of (i) GBT Sole Patents other than Other Royalty Patents, which shall be prosecuted pursuant to Section 7.3, (ii) Joint Patents, which shall be prosecuted pursuant to Section 7.2(c) and Section 7.2(d), and (iii) Other Royalty Patents, which shall be prosecuted pursuant to Section 7.2(d)(v)), as between the Parties, shall have the sole right, but not the obligation, to prosecute with the appropriate patent authorities in the Territory any Patent Rights within the GBT Licensed IP.

(c) **Prosecution of Syros Sole Patents and Joint Patents Prior to Transfer Date**.

(i) As between the Parties, and prior to the Transfer Date, Syros shall have the sole right, but not the obligation, to prosecute all Syros Sole Patents and all Joint Patents in the Territory, at its sole cost and expense and utilizing patent counsel mutually agreed by the Parties. GBT shall provide all information reasonably requested by Syros from time to time in connection with Syros's prosecution of the Joint Patents.

(ii) Syros shall keep GBT reasonably informed as to material developments with respect to the prosecution of the Syros Sole Patents and the Joint Patents. Syros shall provide GBT sufficiently in advance, whenever possible, for GBT to comment, with copies of all patent applications and other material submissions and communications with any patent authorities pertaining to the applicable Patent Rights. Without limitation to Section 7.2(c)(iv), Syros shall consider in good faith all comments and recommendations of GBT with respect to such activities.

(iii) Syros shall not implement any decision to cease prosecution of, abandon or not to continue to pay the expenses of prosecution of, any Syros Sole Patents or Joint Patents in any jurisdiction in the Territory, in each case without the consent of GBT, not to be unreasonably withheld, conditioned or delayed.

(iv) Notwithstanding Sections 7.2(c)(i)-(iii), with respect to each Syros Sole Patent or Joint Patent for which, as of the Option Effective Date, Syros has filed a provisional application with respect to such Patent Right and has not filed a PCT application with respect to such Patent Right, from and after the Option Effective Date until the Transfer Date, Syros shall not file any PCT application and with respect to such Patent Right without the review and consent of GBT, not to be unreasonably withheld, conditioned or delayed.

(d) **Prosecution of Syros Sole Patents and Joint Patents Following the Transfer Date.**

(i) After the Transfer Date, GBT shall have the first right, but not the obligation, to prosecute all Syros Sole Patents and all Joint Patents in the Territory, at its sole cost and expense, and utilizing patent counsel mutually agreed by the Parties. Syros shall provide all information reasonably requested by GBT from time to time in connection with GBT's prosecution of the Syros Sole Patents and the Joint Patents.

(ii) GBT shall keep Syros reasonably informed as to material developments with respect to the prosecution of the Syros Sole Patents and the Joint Patents. GBT shall provide Syros sufficiently in advance, whenever possible, for Syros to comment, with copies of all patent applications and other material submissions and communications with any patent authorities pertaining to the applicable Patent Rights. Without limitation to Section 7.2(d)(iv), GBT shall consider in good faith all comments and recommendations of Syros with respect to such activities. GBT shall not narrow the scope of any claims of any Syros Sole Patent or Joint Patent in any manner that would (A) circumvent or negate any royalty obligation under Section 6.6 or (B) decrease the amount or duration of any royalty payments to Syros under Section 6.6, in each case ((A) or (B)), unless the Parties mutually agree in advance in writing.

(iii) If GBT determines to cease prosecution of, abandon or not to continue to pay the expenses of prosecution of, any Syros Sole Patents or Joint Patents in any jurisdiction in the Territory, GBT shall provide notice thereof to Syros at least [***] prior to any filing or final payment due date, or any other final due date that requires action, in connection with such Syros Sole Patents or Joint Patents. In such event, GBT shall permit Syros, at its discretion and at its sole expense, to continue prosecution of such Syros Sole Patents or Joint Patents. Syros's prosecution of such Syros Sole Patents or Joint Patents shall not change the Parties' respective rights and obligations under this Agreement with respect to such Syros Sole Patents or Joint Patents other than as expressly set forth in this Section 7.2(c)(iii).

(iv) Notwithstanding Sections 7.2(d)(i)-(iii), with respect to each Syros Sole Patent or Joint Patent for which, as of the Transfer Date, Syros has not filed a provisional application or PCT application with respect to such Patent Right, from and after the Transfer Date, GBT shall not file any provisional application or PCT application with respect to such Patent Right without the review and consent of Syros, not to be unreasonably withheld, conditioned or delayed.

(v) With respect to each Other Royalty Patent, from and after the Effective Date, until the expiration the applicable Royalty Term, Sections 7.2(d)(i) – (iii) shall apply to such Other Royalty Patent (*mutatis mutandis* as set forth for Joint Patents). For clarity, 7.2(d)(iv) shall not apply to any Other Royalty Patent.

7.3 Prosecution of GBT Sole Patents other than Other Royalty Patents. GBT shall have the sole right, but not the obligation, to prosecute all GBT Sole Patents that are not Other Royalty Patents, at its sole cost and expense. Until the later of (i) the end of the Research Term and (ii) the Transfer Date:

(a) GBT shall keep Syros reasonably informed as to material developments with respect to the prosecution of the GBT Sole Patents that are not Other Royalty Patents. GBT shall provide Syros sufficiently in advance, whenever possible, for Syros to comment, with copies of all patent applications and other material submissions and communications with any patent authorities pertaining to the applicable Patent Rights; and

(b) GBT shall consider in good faith all comments and recommendations of Syros with respect to such activities. GBT shall not unreasonably implement any decision to cease prosecution of, abandon or not to continue to pay the expenses of prosecution of, any GBT Sole Patents that are not Other Royalty Patents in any jurisdiction in the Territory, in each case without the consent of Syros, not to be unreasonably withheld, conditioned or delayed.

7.4 Consequences of No Option Effective Date. If the Option Exercise Period expires (or is deemed to expire, including pursuant to Section 3.1(d)(iv)) and no Option Effective Date occurs, GBT does hereby, and shall automatically be deemed to, assign to Syros all right title and interest in and to the GBT Sole Inventions, GBT Sole Patents and GBT Sole Know-How, and GBT's interest in all Joint IP at Syros' sole and reasonable expense. Upon such assignment, any and all such Inventions, Know-How and Patent Rights (to the extent not published) shall be deemed to be the Confidential Information of Syros (and not GBT) and Syros shall be deemed to be the Disclosing Party and GBT shall be deemed to be the Receiving Party with respect thereto. Promptly after such expiration or deemed expiration, GBT shall, and shall cause any Affiliates to, without additional compensation, disclose and make available to Syros complete and accurate copies of all pre-clinical and non-clinical data, results of analyses thereof and reports with respect to all Licensed Compounds generated by or on behalf of GBT or its Affiliates prior to such expiration or deemed expiration.

7.5 Cooperation. Each Party shall provide the other Party, at the other Party's request and expense, all reasonable assistance and cooperation in the patent prosecution efforts under Section 7.2, Section 7.3 or Section 7.4, including providing any necessary powers of attorney and executing any other required documents or instruments for such filing, prosecution or maintenance.

7.6 Patent Enforcement.

(a) **Syros Platform Patent Rights and Other Syros Patents**. Syros shall retain all rights to enforce any and all Syros Platform Patents at its sole expense. Syros also shall retain all rights to enforce any Other Syros Patents, at its sole expense, provided that it shall inform GBT in writing to the extent Syros elects to enforce any such Other Syros Patent against any Third Party based upon the use, manufacture, import, sale or offer for sale of any Licensed Compound or Product.

(b) **GBT Sole Patents**. GBT shall retain all rights to enforce any and all GBT Sole Patents, at its sole expense; *provided that*, if such GBT Sole Patents are assigned to Syros pursuant to Section 7.4, Syros shall have and retain all rights to enforce such GBT Sole Patents, at its sole expense.

(c) **Syros Sole Patents and Joint Patents**.

(i) Each Party shall notify the other promptly after becoming aware of (A) any alleged or threatened infringement by a Third Party of any Syros Sole Patents or Joint Patents, including through the using, making, importing, exporting, offering for sale or selling of any Licensed Compound or Product, and including any "patent certification" filed in the United States under 21 U.S.C. §355(b)(2) or 21 U.S.C. §355(j)(2) with respect to any Product or similar provisions in other jurisdictions, or (B) any declaratory judgment action by a Third Party alleging the invalidity, unenforceability or non-infringement of any Syros Sole Patent or Joint Patent (in the case of either (A) or (B), an "**Infringement**").

(ii) Prior to the Option Effective Date, Syros shall have the first right, but not the obligation, to bring and control any legal action to enforce the Syros Sole Patents and Joint Patents in any Infringement, at its own expense and as it reasonably determines appropriate, and GBT shall have the right to be represented in any such action by counsel of its choice. If Syros does not bring such legal action by the earlier of (A) [***] after the notice provided pursuant to Section 7.6(c)(i) or (B) [***] before the time limit, if any, set forth in appropriate laws and regulations for filing of such legal actions, then upon Syros' prior written consent, not to be unreasonably withheld, conditioned or delayed, GBT shall have the right to bring and control any legal action in connection with such infringement, at its own expense.

(iii) Following the Option Effective Date, GBT shall have the first right, but not the obligation, to bring and control any legal action to enforce the Syros Sole Patents and Joint Patents against any Infringement, at its own expense and as it reasonably determines appropriate, and Syros shall have the right to be represented in any such action by counsel of its choice. If GBT does not bring such legal action by the earlier of (A) [***] after the notice provided pursuant to Section 7.6(c)(i) or (B) [***] before the time limit, if any, set forth in appropriate laws and regulations for filing of such legal actions, then upon GBT's prior written consent, not to be unreasonably withheld, conditioned or delayed, Syros shall have the right to bring and control any legal action in connection with such infringement at its own expense.

(d) **Cooperation; Recoveries**.

(i) At the request and expense of the Party bringing the action under Section 7.6(c)(ii) or 7.6(c)(iii), the other Party shall provide reasonable assistance in connection therewith, including by executing reasonably appropriate documents, cooperating in discovery and joining as a party to the action if required. In connection with any such proceeding, the Party bringing the action under Section 7.6(c)(ii) or 7.6(c)(iii) shall not enter into any settlement admitting the invalidity of, or otherwise impairing the other Party's rights in, the Syros Sole Patents, or Joint Patents without the prior written consent of the other Party, which shall not be unreasonably withheld.

(ii) Any recoveries resulting from enforcement action under Section 7.6(c)(ii) or 7.6(c)(iii) shall be first applied against payment of each Party's costs and expenses in connection therewith. Any such recoveries in excess of such costs and expenses shall be shared by the Parties as follows: if GBT is the Party bringing the action, GBT will retain [***] ([***]%)

of such excess recoveries, provided that to the extent that any amounts of such excess recoveries are attributable to lost sales of a Product, such amounts shall be deemed [***], and if Syros is the Party bringing the action, Syros will receive [***] ([***]%) and GBT will receive [***] ([***]%) of such excess recoveries.

7.7 Orange Book Listing. GBT shall have the sole right to determine which Patent Rights (including Syros Sole Patents, GBT Sole Patents, Joint Patents or other Patent Rights) will be submitted for inclusion in the Orange Book maintained by the FDA or similar or equivalent patent listing source, if any, in other countries in the Territory for Products; *provided that* GBT shall have no right to list any Patent Rights within the Syros Excluded IP. Syros will provide all assistance reasonably requested by GBT in connection with such listing, at GBT's reasonable expense.

7.8 Patent Term Extensions. The Parties shall cooperate in obtaining patent term restoration (under but not limited to the U.S. Drug Price Competition and Patent Term Restoration Act and its foreign equivalents), supplemental protection certificates or their equivalents, and patent term extensions with respect to the Syros Sole Patents and Joint Patents in any country and/or region where applicable. GBT shall determine in its sole discretion which Patent Rights (including Syros Sole Patents, Joint Patents, GBT Patents and other Patent Rights but excluding any Patent Rights within the Syros Excluded IP) it shall apply to extend in any country or region in the Territory for any Product, and shall file for such extension at GBT's cost and expense. Syros shall provide all assistance reasonably requested by GBT in connection with such filings, at GBT's reasonable expense.

7.9 Third Party Technology. If in the reasonable opinion of GBT, the Development, manufacture, use or Commercialization of any Licensed Compound or any Product by GBT or any of its Affiliates or its and their respective sublicensees in any country in the Territory infringes or misappropriates, or is reasonably expected to infringe or misappropriate, any Patent Rights, trade secret, or other intellectual property right of a Third Party in such country, then GBT shall have the first right, but not the obligation, to negotiate and obtain a license from such Third Party as necessary for GBT and its Affiliates and its and their respective sublicensees to so exploit such Licensed Compound or Product in such country. If, pursuant to the immediately foregoing sentence, GBT obtains a license from a Third Party under Patent Rights owned or otherwise controlled by such Third Party in a particular country, GBT shall be entitled to deduct from any royalties payable in respect of a calendar quarter under Section 6.6 with respect to such country, [***] ([***]%) of all royalties paid in respect of such calendar quarter and country to such Third Party in respect of such license ("**Third Party Payments**"); provided, however, that such deduction shall not decrease any royalties payable hereunder in respect of such calendar quarter and country by more than [***] ([***]%) and any such deduction shall be subject to Section 6.6(e); and provided, further, that, subject to the foregoing proviso, any Third Party Payments that are not used by GBT in a particular calendar quarter to reduce the applicable royalties payable to Syros hereunder in such calendar quarter may be carried over to subsequent calendar quarters until fully used in accordance with this Section 7.9.

7.10 Trademarks. GBT shall have the right in its sole discretion to brand Products using GBT related trademarks and any other trademarks and trade names it determines appropriate,

which may vary by country or within a country ("**Product Marks**"). GBT shall own all rights in the Product Marks and shall have the sole right to register and maintain the Product Marks in the countries and regions that it determines, at GBT's cost and expense.

ARTICLE 8
REPRESENTATIONS, WARRANTIES, AND COVENANTS

8.1 Mutual Representations and Warranties. Each Party hereby represents and warrants to the other Party as follows as of the Effective Date:

(a) **Corporate Existence**. It is a corporation duly organized, validly existing, and in good standing under the Laws of the jurisdiction in which it is incorporated.

(b) **Corporate Power, Authority; No Conflict**. The execution and delivery of this Agreement and the performance by it of the transactions contemplated hereby have been duly authorized by all necessary corporate action, and do not violate: (i) such Party's charter documents, bylaws, or other organizational documents; (ii) any agreement, instrument, or contractual obligation to which such Party is bound; (iii) any requirement of any applicable Law; or (iv) any order, writ, judgment, injunction, decree, determination, or award of any court or Government Authority presently in effect applicable to such Party.

(c) **Legally Binding**. This Agreement is a legal, valid, and binding obligation of such Party enforceable against it in accordance with its terms and conditions.

8.2 Additional Representations and Warranties of Syros. Syros represents and warrants to GBT as follows as of the Effective Date:

(a) **Title; Encumbrances.** Syros is the sole owner of the entire right, title and interest in and to all Patent Rights and Know-How within the Licensed IP that exist as of the Effective Date, free and clear from any mortgages, pledges, liens, security interests, conditional and installment sale agreements, encumbrances, charges or claims of any kind.

(b) **Rights and Licenses.** Syros has the right to grant the applicable rights and licenses provided for under this Agreement and to perform the activities allocated to it under the Research Plan as set forth in **Exhibit A.**

(c) **No Patents**. Except for the Patent Rights set forth in **Exhibit D**, to Syros's knowledge, Syros does not own or Control, as of the Effective Date, any Patent Rights that specifically recite the composition or method of use or manufacture of any compound that modulates any Collaboration Target.

(d) **Syros Platform.** Syros has not received any notice or threat from any Third Party asserting or alleging that any use of the Syros Platform or the Syros Platform IP prior to the Effective Date misappropriated the intellectual property rights of such Third Party. No claim or litigation has been brought or threatened by any Person alleging, and neither Syros nor any of its Affiliates has any knowledge of any threatened claim alleging, that the conception, development, or use of the Syros Platform as of the Effective Date or as anticipated to be used in the conduct of the Research Program as set forth in **Exhibit A** infringes any Patent Rights of any Third Party.

(e) **Third Party Technology**. To Syros's knowledge, the use by Syros of the Syros Platform to conduct the Research Plan as set forth in **Exhibit A** will not infringe any issued patents of a Third Party, and there are no pending Third Party patent applications that, if issued with the published or currently pending claims, would be infringed by any such use.

(f) **Upstream Obligations**. There are no amounts that will be required to be paid by Syros to a Third Party under a license agreement between Syros and such Third Party existing as of the Effective Date as a result of Syros's conduct of the Research Plan as set forth in **Exhibit A**.

8.3 Mutual Covenants. Each Party covenants to the other Party as follows:

(a) **No Debarment**. In the course of its activities under this Agreement, neither Party shall use any employee or contractor who has been debarred by any Regulatory Authority or, to such Party's knowledge, is the subject of debarment proceedings by a Regulatory Authority. Each Party shall notify the other Party promptly upon becoming aware that any of its employees or consultants has been debarred or is the subject of debarment proceedings by any Regulatory Authority.

(b) **Compliance**. Each Party and its Affiliates shall comply in all material respects with all applicable Laws in the performance of its obligations and practice of its rights under this Agreement.

(c) **Non-Encumbrance**. During the Term, Syros and its Affiliates shall not sell or assign to any Third Party Patent Rights or Know-How within the Licensed IP, and GBT and its Affiliates shall not sell or assign to any Third Party Patent Rights or Know-How within the GBT Licensed IP or that would be within the scope of license rights granted to Syros upon termination pursuant to Section 11.3(b)(i), in each case, without the other Party's consent; provided that neither Party shall be prohibited under this Section 8.3(c) (or shall be in breach of this Section 8.3(c)) due to (i) the grant by such Party or its Affiliate of any Permitted Lien with respect to the applicable Patent Rights or Know-How or (ii) a Change of Control of such Party or any of its Affiliates.

8.4 Disclaimer. EXCEPT AS EXPRESSLY STATED IN THIS AGREEMENT, NO REPRESENTATIONS OR WARRANTIES WHATSOEVER, WHETHER EXPRESS OR IMPLIED OR WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NON-INFRINGEMENT OR NON-MISAPPROPRIATION OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS OR WARRANTIES REGARDING ACHIEVEMENT OF ANY OBJECTIVES OF THE RESEARCH PROGRAM, APPROVAL OR COMMERCIAL POTENTIAL OF ANY PRODUCT, OR IDENTIFICATION OR USEFULNESS OF ANY COLLABORATION TARGETS, COLLABORATION COMPOUNDS, OR IND CANDIDATES, ARE MADE OR GIVEN BY OR ON BEHALF OF A PARTY, AND, EXCEPT AS EXPRESSLY STATED IN THIS AGREEMENT, ALL REPRESENTATIONS AND WARRANTIES, WHETHER EXPRESS OR IMPLIED AND WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE, ARE HEREBY EXPRESSLY EXCLUDED.

ARTICLE 9
INDEMNIFICATION

9.1 Indemnification by Syros. Syros shall defend, indemnify, and hold GBT and its Affiliates and its and their respective officers, directors, employees and agents (the "**GBT Indemnitees**") harmless from and against any and all losses, damages, liabilities, costs and expenses (including reasonable attorneys' fees and expenses) (collectively, "**Losses**") in connection with any and all suits, proceedings, investigations, causes of action or claims of Third Parties (collectively, "**Claims**") to the extent arising or resulting from: (a) the conduct of the Research Program by or on behalf of Syros or any other Syros Indemnitees; (b) the negligence or willful misconduct of Syros or any other Syros Indemnitees; (c) the breach by Syros of any covenant, representation, warranty or other agreement made by Syros in this Agreement; or (d) the Development, manufacture or Commercialization of Licensed Compounds or Products by or on behalf of Syros or its licensees or any other Syros Indemnitee after termination of this Agreement; except, in each case (a)-(d), to the extent such Claims result from the breach by GBT of any covenant, representation, warranty or other agreement made by GBT in this Agreement or the negligence or willful misconduct of GBT or any other GBT Indemnitee.

9.2 Indemnification by GBT. GBT shall defend, indemnify, and hold Syros and its Affiliates and its and their respective officers, directors, employees and agents (the "**Syros Indemnitees**") harmless from and against any and all Losses in connection with any and all Claims to the extent arising or resulting from: (a) the conduct of the Research Program by or on behalf of GBT or any other GBT Indemnitees; (b) the Development, manufacture or Commercialization of Licensed Compounds or Products by or on behalf of GBT or its sublicensees or any other GBT Indemnitee; (c) the negligence or willful misconduct of GBT or any other GBT Indemnitees; or (d) the breach by GBT of any covenant, representation, warranty or other agreement made by GBT in this Agreement; except, in each case (a)-(d), to the extent such Claims result from the breach by Syros of any covenant, representation, warranty or other agreement made by Syros in this Agreement or the negligence or willful misconduct of Syros or any other Syros Indemnitee.

9.3 Indemnification Procedure. If either Party is seeking indemnification under Section 9.1 or 9.2 (the "**Indemnified Party**"), it shall notify the other Party (the "**Indemnifying Party**") of the Loss giving rise to the obligation to indemnify pursuant to such Section as soon as reasonably practicable after becoming aware of such Loss, but in no event shall the Indemnifying Party be liable for any Losses that result from any delay in providing such notice. The Indemnifying Party shall have the right, upon notice to the Indemnified Party, to assume the defense of any Claim for which it is obligated to indemnify the Indemnified Party, including the right to select counsel of its choosing and the right to compromise or settle such Claim, *provided* that the Indemnifying Party shall not make any compromise or settlement admitting fault, subjecting the Indemnified Party to injunctive or other relief, or incurring any liability on the part of the Indemnified Party or any GBT Indemnitee or Syros Indemnitee, as applicable, without the Indemnified Party's prior written consent, such consent not to be unreasonably withheld or delayed. The Indemnified Party shall cooperate with the Indemnifying Party and the Indemnifying Party's insurer as the Indemnifying Party may reasonably request, and at the Indemnifying Party's cost and expense. The Indemnified Party shall have the right to participate, at its own expense and with counsel of its choice, in the defense of any Claim the defense of which has been assumed by the Indemnifying Party pursuant to this Section 9.3.

ARTICLE 10
CONFIDENTIALITY; PUBLICATION

10.1 Duty of Confidence. Subject to the other provisions of this Article 11:

(a) all Confidential Information of a Party or its Affiliates (collectively, the "**Disclosing Party**") under this Agreement shall be maintained in confidence and otherwise safeguarded by the other Party (the "**Receiving Party**") and its Affiliates, in the same manner and with the same protection as such Receiving Party maintains its own confidential information;

(b) the Receiving Party may only use any such Confidential Information for the purposes of performing its obligations or exercising its license, ownership, retained or other rights under this Agreement; and

(c) the Receiving Party may disclose Confidential Information of the Disclosing Party to its and its Affiliates' employees, directors, agents, contractors (to the extent permitted hereunder), consultants and advisers of the Receiving Party, in each case to the extent reasonably necessary for the purposes of, and for those matters undertaken pursuant to, this Agreement (including exercising rights and fulfilling obligations); provided that such Persons are bound by a written contract, a fiduciary duty or an ethical obligation of an attorney to maintain the confidentiality of such Confidential Information and to use the Confidential Information in a manner consistent with the confidentiality provisions of this Agreement.

10.2 Exceptions. The foregoing obligations as to particular Confidential Information of a Disclosing Party shall not apply to the extent that the Receiving Party can demonstrate that such Confidential Information:

(a) is known by the Receiving Party at the time of its receipt without an obligation of confidentiality, and not through a prior disclosure by the Disclosing Party, as documented by the Receiving Party's business records, provided that the foregoing exception shall not apply with respect to any Confidential Information that is deemed to be the Confidential Information of a Party pursuant to the proviso in the definition of "Confidential Information" or pursuant to Section 7.4 or Section 11.3(b)(iii), regardless of whether such Confidential Information was in the Receiving Party's possession prior to such disclosure;

(b) is in the public domain before its receipt from the Disclosing Party, or thereafter enters the public domain through no fault of the Receiving Party;

(c) is subsequently disclosed to the Receiving Party by a Third Party who may lawfully do so and is not under an obligation of confidentiality to the Disclosing Party; or

(d) is developed by the Receiving Party independently and without use of, or reference to, any Confidential Information received from the Disclosing Party, as documented by the Receiving Party's business records, provided that the foregoing exception shall not apply with respect to any Confidential Information that is deemed to be the Confidential Information of a Party pursuant to the proviso (x) and (y) in the definition of "Confidential Information" or pursuant to Section 7.4 or Section 11.3(b)(iii), regardless of whether such Confidential Information was in the Receiving Party's possession prior to such disclosure, except that this exception shall not apply

with respect to any such independent development that occurs following the date upon which such information is deemed to be Confidential Information of a Party pursuant to Section 7.4 or Section 11.3(b)(iii).

Any combination of features or disclosures shall not be deemed to fall within the foregoing exclusions merely because individual features are published or available to the general public or in the rightful possession of the Receiving Party unless the combination itself and principle of operation are published or available to the general public or in the rightful possession of the Receiving Party.

10.3 Authorized Disclosures. Notwithstanding the obligations set forth in Sections 10.1 and 10.6, the Receiving Party may disclose Disclosing Party's Confidential Information to the extent such disclosure is reasonably necessary in the following instances:

(a) filing or prosecuting Patent Rights as permitted by this Agreement;

(b) prosecuting or defending litigation as permitted by this Agreement;

(c) complying with the listing rules of any exchange on which the Receiving Party's or its Affiliate's securities are traded;

(d) in Regulatory Materials that the Receiving Party has the right to make under this Agreement;

(e) to actual or potential: investors, acquirors, sublicensees and other financial or commercial partners solely for the purpose of evaluating or carrying out an actual or potential investment, acquisition, sublicense or collaboration; provided that in each such case on the condition that such recipients are bound by confidentiality and non-use obligations substantially consistent with those contained in the Agreement (except that the term may be shorter with respect to potential investors); or

(f) as required by Law, judicial or administrative process, provided that in such event such Party shall promptly inform the other Party of such required disclosure and provide the other Party an opportunity to challenge or limit the disclosure obligations. Confidential Information that is disclosed pursuant to this Section 10.3(f) shall remain otherwise subject to the confidentiality and non-use provisions of this Article 10, and the Party disclosing Confidential Information pursuant to Law or court order shall take all steps reasonably necessary, including seeking of confidential treatment or a protective order to ensure the continued confidential treatment of such Confidential Information; or

(g) subject to Section 10.5, in the case of any Joint Know-How (excluding Joint Know-How consisting of (A) the composition of any Licensed Compound, (B) structural or SAR data for any Licensed Compound or (C) except to the extent disclosed in the joint press release set forth in Exhibit B or otherwise agreed in writing by the Parties, the role of any Collaboration Target in the up-regulation of fetal hemoglobin), notwithstanding anything contained in Section 10.1 or Section 10.6, each Party shall have a right to disclose such Joint Know-How for uses other than the Development, making, having made (including manufacture and having manufactured), use, sale, offer for sale, import, export or other exploitation of Licensed Compounds and Products in

the Field in the Territory; *provided that* such Party exercises reasonable business practices in disclosing such Joint Know-How in the same manner and with the same protections as it utilizes in disclosing other of its confidential information.

10.4 Inventions and Program Know-How. Notwithstanding the obligations set forth in Sections 10.1 and 10.6, after the Option Effective Date, GBT shall have the right to disclose to any Person, any Confidential Information to the extent consisting of Inventions or Program Know-How for which GBT makes a good faith determination that such use or disclosure is necessary or reasonably useful to Develop, make, have made (including manufacture and have manufactured), use, sell, offer for sale, import, export or otherwise exploit any Licensed Compound or Product; provided that in each such case on the condition that such recipients are bound by confidentiality and non-use obligations substantially consistent with those contained in the Agreement (except that the term may be shorter).

10.5 Scientific Publication. Prior to the Option Effective Date, neither Party shall publish or publicly present any results of studies carried out under this Agreement related to Collaboration Targets, Collaboration Compounds, Licensed Compounds or Products without the prior written approval of the other Party, which the other Party may grant or withhold in its sole discretion. After the Option Effective Date, (a) Syros shall not publish or otherwise publicly present any results of studies carried out under this Agreement related to Licensed Compounds or Products without the prior written approval of GBT, which GBT may grant or withhold in its sole discretion, and (b) nothing in this Agreement will restrict, or be deemed to restrict, GBT from publishing or presenting the results of any studies conducted hereunder related to Licensed Compounds or Products, provided that prior to any publication or presentation of the results of any studies conducted under the Research Program, GBT shall provide Syros with the manuscript or proposed publication presentation of such studies and consider Syros' comments in good faith. Notwithstanding the foregoing, and subject to the terms of this Article 10, no Confidential Information of a Party may be published or publicly presented by the other Party without such other Party's prior written approval, which may be granted or withheld by such other Party in its sole discretion, provided that after the Option Effective Date, Syros' approval is not required for GBT to publish or present Confidential Information of Syros to the extent consisting of Inventions or Program Know-How. When a copy of any manuscript or proposed publication or presentation is provided by the publishing Party to the other Party for review or approval, as applicable, the other Party shall review and provide its comments to the publishing or presenting Party within [***] of the receipt of such copy. With respect to publications and presentations of either Party prior to the Option Effective Date, and with respect to publications and presentations of Syros after the Option Effective Date, failure to respond within such [***] shall be deemed approval to publish or present or no comments from such other Party hereunder.

10.6 Publicity; Terms of Agreement.

(a) The Parties agree that the terms of this Agreement are the Confidential Information of both Parties, subject to the special authorized disclosure provisions set forth in this Section 10.6 or Section 10.3.

(b) GBT and Syros have agreed on language of a joint press release announcing this Agreement, which is attached hereto as **Exhibit B**, to be issued by the Parties promptly after the Effective Date.

(c) Except for such press release, neither Party shall make any public disclosure concerning the material terms of this Agreement or any activities under the Research Program without the prior written approval of such disclosure by the other Party, except that approval shall not be required for public governmental filing or disclosure required by Law (but in such case the comments of the other Party shall be considered in good faith). Accordingly, if either Party desires to make a public disclosure (including disclosure required by Law) concerning the material terms of this Agreement or any activities under the Research Program, such Party shall provide a copy of the proposed text of such disclosure to the other Party at least [***] in advance of such disclosure (except to the extent a shorter period is required to comply with applicable Law). Each such disclosure shall contain appropriate references to the other Party if so requested. A Party commenting on such a proposed disclosure shall provide its comments, if any, within [***] after receiving the proposed disclosure for review, and the Parties shall thereafter discuss in good faith and agree on any such disclosure (except for disclosure required by Law). Neither Party shall be required to seek the permission of the other Party to repeat any information that has already been publicly disclosed by such Party, or by the other Party, in accordance with this Section 10.6(c), provided such information remains accurate as of such time.

(d) The Parties acknowledge that either or both Parties may be obligated to file under applicable Laws a copy of this Agreement with the U.S. Securities and Exchange Commission or other Governmental Authorities. Each Party shall be entitled to make such a required filing, provided that it uses [***] to maintain the confidentiality of the terms of this Agreement in any such filing or disclosure, to the extent such confidential treatment is reasonably available to such Party. In the event of any such filing, each Party will provide the other Party with a copy of this Agreement marked to show provisions for which such Party intends to seek confidential treatment and shall reasonably consider the other Party's reasonable comments thereon to the extent consistent with the filing Party's legal requirements and obligations governing disclosure of material agreements and material information that must be publicly filed.

ARTICLE 11
TERM AND TERMINATION

11.1 Term. The term of this Agreement (the "**Term**") shall commence on the Effective Date and, unless earlier terminated pursuant to Section 11.2, shall continue until the expiration of the last to expire Royalty Term for any Product in the Territory. Upon the expiration (but not early termination pursuant to Section 11.2) of the Royalty Term for a particular Product and country, the license granted by Syros to GBT under Section 3.2(a) with respect to such Product and country shall become non-exclusive, fully-paid, royalty free, perpetual and irrevocable.

11.2 Termination.

(a) **Termination of Research Program for Willful Misconduct.** GBT may terminate the Research Program and the Research Term upon written notice to Syros if Syros

materially breaches this Agreement as a result of willful misconduct with regard to its obligations under Section 2.6; provided that Syros shall have an opportunity to cure or to dispute such alleged material breach and willful misconduct (*mutatis mutandis* as set forth with respect to any material breach of this Agreement covered by Section 11.2(c), except that the cure period will be [***] and will not be extendible). Upon the effective date of termination of the Research Program and Research Term pursuant to this Section 11.2(a), without limiting any other rights or remedies that may be available to GBT, the following consequences will apply: (i) GBT shall have no obligations to reimburse Syros under Sections 2.5 and 6.2 (except for amounts incurred prior to termination for activities properly conducted); (ii) GBT's obligations under Section 3.6(a) will immediately terminate; (iii) the Parties' obligations to form a JDC will immediately terminate; and (iv) Syros' Co-Detailing Option under Section 5.8 will immediately terminate. For clarity, termination of the Research Program and Research Term by GBT hereunder is not a termination of this Agreement, and GBT will retain the right to exercise its Option pursuant to Section 3.1, subject, for clarity, to its obligation to use Commercially Reasonable Efforts pursuant to Section 5.2 if GBT exercises its Option and to GBT's other non-terminated obligations under this Agreement.

(b) **Unilateral Termination by GBT.** GBT may terminate this Agreement in its entirety, for any or no reason, upon (i) nine (9) months' prior written notice if the effective date of such termination is during the Research Term; (ii) ninety (90) days' prior written notice to Syros if the effective date of such termination is after the expiration or termination of the Research Term; or (iii) [***] prior written notice to Syros at any time following a Change of Control of Syros (whether during the Research Term or following expiration or termination of the Research Term).

(c) **Termination by Either Party for Breach**.

(i) **Breach.** Subject to Section 11.2(c)(ii), each Party shall have the right to terminate this Agreement upon written notice to the other Party if such other Party materially breaches this Agreement and, after receiving such written notice from the non-breaching Party identifying such material breach in reasonable detail, fails to cure such material breach within [***] (or, with respect to breach of any payment obligations by GBT, [***]) from the date of such notice, provided, however, that if any breach other than a payment breach is not reasonably curable within [***] and if the alleged breaching Party is making a bona fide effort to cure such breach, such termination will be delayed for a reasonable period of time (not to exceed [***]) from the date of the breach notice provided hereunder) to allow the alleged breaching Party to cure such breach.

(ii) **Disputed Breach.** If the alleged breaching Party disputes in good faith the existence or materiality of a breach specified in a notice provided by the other Party in accordance with Section 11.2(c)(i), and such alleged breaching Party provides the other Party notice of such dispute within the [***] (or, with respect to a payment breach, [***]) cure period, then the non-breaching Party shall not have the right to terminate this Agreement under Section 11.2(c)(i) unless and until the arbitrators, in accordance with Section 12.7, have determined that the alleged breaching Party has materially breached this Agreement and such Party fails to cure such breach within [***] (or, with respect to a payment breach, [***]) following such arbitrators' decision. It is understood and agreed that

during the pendency of such dispute, all of the terms and conditions of this Agreement shall remain in effect and the Parties shall continue to perform all of their respective obligations hereunder.

(d) **Termination for Insolvency**. Each Party will have the right to terminate this Agreement immediately upon written notice if: (i) the other Party becomes insolvent; (ii) the other Party files a petition in bankruptcy, or an involuntary petition in bankruptcy is filed against the other Party and the other Party consents to such petition, or such involuntary petition is not dismissed within [***] and the other Party (A) fails to assume this Agreement in any such bankruptcy proceeding within [***] after filing or (B) assumes and assigns this Agreement to a Third Party; or (iii) a receiver or guardian has been appointed for the other Party who is not discharged within [***] after appointment.

(e) **Termination for Failure to Exercise Option**. In the event the Option Period expires without GBT having timely delivered an Option Exercise Notice, or in the event that the Option Exercise Period is deemed to expire pursuant to Section 3.1(d)(iv), this Agreement shall terminate in its entirety without need for any notice from either Party to the other.

(f) **Termination for Patent Challenge**. If GBT or any of its Affiliates, anywhere in the Territory, institutes, prosecutes or otherwise participates in (or in any way aids any Third Party in instituting, prosecuting or participating in), at law or in equity or before any administrative or regulatory body, including the U.S. Patent and Trademark Office or its foreign counterparts, any claim, demand, action or cause of action for declaratory relief, damages or any other remedy or for an enjoinment, injunction or any other equitable remedy, including any interference, re-examination, opposition or any similar proceeding, alleging that any claim in any Patent Rights within the Licensed IP is invalid, unenforceable or otherwise not patentable, Syros shall have the right to terminate this Agreement in its entirety upon [***] prior written notice to GBT; provided that such termination will not be effective if GBT or its Affiliate withdraws the applicable claim, demand, action, cause of action or other proceeding within such [***] period. GBT will include an equivalent provision to this Section 11.2(f) in each sublicense agreement with any sublicensees to which GBT has granted Development or Commercialization rights with respect to a Licensed Compound or Product and for which Syros has received notice pursuant to Section 3.2(c), and shall enforce its rights under such provision by terminating the sublicense for failure to withdraw the claim within [***] following such sublicensee's receipt of written notice to withdraw such claim from GBT. The foregoing will not apply to, and Syros will not have a termination right on account of: (i) activities in the normal course of patent prosecution, (ii) defense to a claim, including a counter-claim, first brought by Syros or any of its Affiliates or licensees, (iii) responding to compulsory discovery, subpoenas or other requests for information in a judicial or arbitration proceeding or (iv) complying with any applicable law, regulation or court order.

11.3 Effects of Termination.

(a) Upon the termination of this Agreement for any reason, all licenses and other rights granted to GBT under the Licensed IP, and all sublicenses granted thereunder, shall terminate.

(b) In addition, if this Agreement is terminated (i) by GBT pursuant to Section 11.2(b) or (ii) by Syros pursuant to Section 11.2(c), Section 11.2(d) or Section 11.2(f), then:

(i) GBT hereby grants to Syros, effective as of the effective date of such termination, a worldwide, exclusive, royalty-bearing (only to the extent as provided in Section 11.3(b)(ii) below) license, with the right to grant sublicenses through multiple tiers, under (A) those Patent Rights and Know-How Controlled by GBT or any of its Affiliates, or its or their sublicensees that are necessary for, or were used by GBT or its Affiliates or sublicensees for, the Development, manufacture or Commercialization of Licensed Compounds or Products and (B) without limitation to clause (A), GBT Sole Inventions, GBT Sole Know-How, GBT Sole Patents, and GBT's interests in and to any Joint IP to research, Develop, make, have made (including manufacture and have manufactured), use, sell, offer for sale, import, export and otherwise Commercialize Licensed Compounds or Products in the Field in the Territory; provided that: (1) if any such Patent Right or Know-How was in-licensed or acquired by GBT or any of its Affiliates or its or their sublicensees from a Third Party and is subject to payment or other obligations to such Third Party, GBT shall promptly disclose such obligations to Syros in writing and such Patent Right shall be subject to the license granted in this Section only to the extent Syros agrees in writing to be bound by such obligations and reimburse all amounts owed to such Third Party as a result of Syros's exercise of such license with respect to such Patent Right or Know-How; and (2) the Patent Rights licensed to Syros pursuant to this Section shall not include any proprietary manufacturing, formulation or drug delivery technology or any other technology of GBT that was not used by or on behalf of GBT or any of its Affiliates or its or their sublicensees in the production, manufacture or Development of any Licensed Compound or Product.

(ii) In consideration for such license granted in Section 11.3(b)(i), and solely if the effective date of such termination occurs after milestone event number 1 set forth in Section 6.4(a) has been achieved, Syros shall pay to GBT royalties, on a Product-by-Product basis, on any net sales (defined *mutatis mutandis* with the definition of Net Sales in this Agreement) by Syros, its Affiliates or its sublicensees of such Product for any and all uses in the Field in the Territory as calculated by multiplying the applicable royalty rate set forth in the table below by the aggregated annual Net Sales of such Product in the Territory in the applicable calendar year. Royalty rates will be determined by the development stage of the Product on the effective date of termination.

Effective Date of Termination Occurs	**Royalty Rate**
After [***] but prior to [***]	[***]%
After [***] but before [***]	[***]%
After [***]	[***]%

The terms of Sections 6.6, 6.8, 6.9, 6.10 and 7.9 and the definitions of Royalty Term and Net Sales will apply to the payment and reporting of such royalties by Syros, *mutatis mutandis*.

(iii) GBT shall and hereby does, and shall cause its Affiliates and its and their sublicensees to, effective as of the effective date of termination, assign and transfer to Syros all Regulatory Materials and Regulatory Approvals and copies of all clinical and nonclinical data specific to Licensed Compounds or Products in the Territory that are Controlled by GBT, any of its Affiliates, or its or their sublicensees. GBT shall, and shall procure that its Affiliates shall, take such actions and execute such instruments, assignments and documents as may be reasonably requested by Syros, at Syros' reasonable expense, to effect fully the transfer of rights under such Regulatory Materials and Regulatory Approvals to Syros. If applicable Law prevents or delays the transfer of ownership of any such Regulatory Materials or Regulatory Approvals to Syros, GBT shall maintain at Syros' request, and shall grant, and does hereby grant, to Syros, and at Syros' request, its designees, an exclusive and irrevocable right of access and reference to such Regulatory Materials and Regulatory Approvals for the Licensed Compounds and Products in the Territory, and shall cooperate with Syros to make the benefits of such Regulatory Materials and Regulatory Approvals available to Syros or its designee(s) with effect from the effective date of such termination. Effective as of the effective date of termination, any and all such Regulatory Materials and Regulatory Approvals (to the extent not published) shall be deemed to be the Confidential Information of Syros (and not GBT) and Syros shall be deemed to be the Disclosing Party and GBT shall be deemed to be the Receiving Party with respect thereto.

(iv) Following receipt of a written request and reasonable transfer instructions from Syros, GBT shall deliver to Syros all safety data contained in the global safety database for the Licensed Compounds and Products and transfer control of and responsibility for maintaining the global safety database to Syros, at Syros' reasonable expense.

(v) If GBT is, as of the effective date of termination of the Agreement, party to any material subcontracts that pertain solely to the manufacture of Licensed Compounds or Products in the Territory, then GBT will use reasonable efforts [***].

(vi) GBT shall transfer to Syros, at Syros's request, any remaining inventory of the Licensed Compounds and Products, and components thereof and raw materials used by or on behalf of GBT in the manufacture of the Licensed Compounds and Products that, in each case, are in GBT's or its Affiliate's possession as of the effective date of termination at a price [***]. Within [***] after the effective date of termination (or within [***] after such later date described in the preceding proviso, if applicable), GBT shall notify Syros (A) of the quantity(ies) and type(s) of the remaining inventory and the cost thereof and (B) whether any such inventory will need to be relabeled or repackaged to remove any GBT housemarks, and Syros shall have [***] after receipt of such notice to notify GBT of the quantity(ies) and type(s) of the remaining inventory that Syros wishes to acquire. If Syros does not so notify GBT within the applicable period specified above, or notifies GBT within the applicable period specified above that Syros elects to purchase less than all of the remaining inventory, then GBT shall be entitled to elect to continue to sell such inventory

for up to [***] after the effective date of termination, or to destroy such inventory; provided, however, that any inventory that is sold by GBT after the effective date of termination pursuant to this Section shall be subject to payment of royalties pursuant to Section 6.6.

(vii) Without limitation to Syros' rights under Section 11.3(b)(v), at a time reasonably requested by Syros, which request shall in any event be made no later than [***] following the effective date of termination, the Parties shall cooperate to facilitate a transfer of the relevant manufacturing process for the Licensed Compounds and Products then being conducted by GBT and any of its Affiliates or Third Party subcontractors to Syros or its designee. In the case of any such requests, GBT shall exercise its rights under the terms of any applicable upstream manufacturing agreement between GBT and the Third Party manufacturer to require the Third Party manufacturer to conduct such transfer pursuant to the terms and conditions of the applicable agreement, if such agreement entitles GBT to receive or direct a technology transfer consistent with the Third Party manufacturer's customary transfer standard operating procedure or as otherwise provided in the applicable agreement. GBT shall provide reasonable assistance to Syros in connection with such manufacturing transfer by making GBT's technical personnel who are knowledgeable about the manufacturing process reasonably available to Syros for consultation and, if applicable, introducing Syros to GBT's Third Party manufacturer(s) for the Licensed Compounds and Products. Except in the event of termination by Syros pursuant to Section 11.2(c), Syros shall reimburse all reasonable and documented out-of-pocket costs incurred by GBT to conduct and assist Syros with any such requested transfer.

(viii) If, at the date of notice of termination, any clinical trial is being conducted by GBT with respect to any Licensed Compounds or Products in the Territory, then Syros shall notify GBT in writing within [***] after the notice of termination whether [***].

(ix) Upon written request of Syros, GBT shall cause to be assigned to Syros all rights in and to any Product Marks solely relating to the Licensed Compounds or Products in the Territory. Until the effective date of such assignment, GBT hereby grants to Syros, effective as of the effective date of such termination, a worldwide, exclusive, royalty-free license, with the right to grant sublicenses through multiple tiers, under such Product Marks to research, Develop, make, have made (including manufacture and have manufactured), use, sell, offer for sale, import, export and otherwise Commercialize Licensed Compounds or Products in the Field in the

Territory, provided that GBT shall have the retained right to use such Product Marks pursuant to the last sentence of Section 11.3(b)(vi).

(x) Notwithstanding anything to the contrary herein, if any Product is a Combination Product, then GBT shall not be obligated to grant any licenses or other rights or provide or assign any Regulatory Materials, data or tangible materials to Syros with respect to the Other Products therein. For clarity, all licenses and other rights granted to GBT under the Licensed IP shall terminate with respect to any Combination Product upon termination of this Agreement for any reason.

(c) Upon any termination of this Agreement, all Confidential Information of GBT that is licensed to Syros under Section 11.3(b)(i) to the extent relating to any Licensed Compound or Product (except in the case of any Combination Product to the extent relating to Other Products therein) shall become Confidential Information of Syros.

(d) Upon termination of this Agreement, each Party shall promptly return to the other Party, or destroy and certify such destruction in writing, all Confidential Information of such other Party for which such first Party does not have an ownership interest, a continuing license or other right to use such Confidential Information after termination of this Agreement.

11.4 Terminated Sublicenses. Without limitation to Section 11.3(a), if this Agreement is terminated by Syros pursuant to Section 11.2(c) or Section 11.2(d) and, as of the effective date of termination, one or more sublicense agreements was then in effect between GBT and a Third Party under which GBT had granted Development or Commercialization rights with respect to a Licensed Compound or Product and for which Syros had received timely notice pursuant to Section 3.2(c), in the event that Syros' receives from any such applicable Third Party (other than any such Third Party that has materially breached, or that GBT alleges has materially breached, its sublicense agreement with GBT) within [***] following the effective date of termination of this Agreement a written request for Syros to consider granting to such Third Party a direct license with the same scope as the sublicense that had been granted to such Third Party by GBT, Syros shall respond to such request within [***]. The determination of whether to engage in discussions with, or negotiate terms with, any such Third Party shall be within Syros' sole and absolute discretion, and in no event shall Syros have any obligation to enter into such negotiations or grant such license (or any other rights or license) to such Third Party.

11.5 Survival. Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination.

(a) Without limiting the foregoing, the following provisions shall survive termination of this Agreement: Sections 2.5 (for any unreimbursed Approved Costs incurred prior to the effective date of termination (including, to the extent consistent with the Research Budget and Permitted Overages, any reasonable non-cancellable commitments incurred by Syros or its Affiliates or for which Syros or its Affiliates have become obligated for purposes of conducting the Research Program); 2.7 (for a period of at least [***] after termination or such longer period as may be required by law for particular records); 2.9; 2.10 (last sentence only); 3.1(d)(iv) (last two sentences only); 3.2(c) (third sentence, solely with respect to any terms and conditions surviving pursuant to this Section 11.4, and fourth sentence only); 3.7 (solely with respect to

activities prior to the effective date of termination); 5.3 (solely (i) to the extent GBT winds down, or continues to conduct prior to transfer to Syros, any clinical trial with respect to a Licensed Compound or Product following the effective date of termination pursuant to Section 11.3(b)(viii) or (ii) until the completion of any required transfer pursuant to Section 11.3(b) of Development records maintained pursuant to Section 5.3); 5.4 (second sentence only); 5.5(b) (to the extent resulting from activities prior to the effective date of termination or after the effective date of termination pursuant to Section 11.3(b)(vi) or Section 11.3(b)(viii)); 5.7 (first sentence only, solely with respect to the period prior to the effective date of termination or to the extent GBT winds down, or continues to conduct prior to transfer to Syros, any clinical trial with respect to a Licensed Compound or Product following the effective date of termination pursuant to Section 11.3(b)(viii)); 6.2 (for any unreimbursed Approved Costs incurred prior to the effective date of termination (including, to the extent consistent with the Research Budget and Permitted Overages, any reasonable non-cancellable commitments incurred by Syros or its Affiliates or for which Syros or its Affiliates have become obligated for purposes of conducting the Research Program); 6.3 (solely in circumstances in which GBT has exercised the Option prior to the effective date of termination but has not paid the Option Exercise Fee as of such date); 6.4 (solely with respect to any milestone achieved prior to the effective date of termination but with respect to which GBT has not paid the corresponding milestone payment(s) as of such date); 6.5 (solely with respect to Net Sales accrued prior to the effective date of termination or after such date pursuant to Section 11.3(b)(vi)); 6.6 (solely with respect to Net Sales accrued prior to the effective date of termination or after such date pursuant to Section 11.3(b)(vi) or as necessary to give effect to Section 11.3(b)(ii)); 6.7; 6.8-6.9 (for clarity, including with respect to any Net Sales accrued or milestone payments accrued, or other amounts accrued, prior to the effective date of termination or after such date pursuant to Section 11.3(b)(vi) and including as necessary to give effect to 11.3(b)(ii)); 6.10 (solely for the term set forth therein, but for clarity, including with respect to any Net Sales accrued or milestone payments accrued, or other amounts accrued, prior to the effective date of termination or after such date pursuant to Section 11.3(b)(vi), including as necessary to give effect to 11.3(b)(ii)); 7.1(a); 7.1(b); 7.1(c); 7.1(d); 7.1(f); 7.2(a); 7.2(b); 7.2(d)(i)-(iii) (solely in the event the effective date of termination occurs after the Option Effective Date, and solely with respect to (i) Joint Patents and (ii) GBT Sole Patents and Other Royalty Patents as if such Patent Rights were Joint Patents, in each case ((i) or (ii)), except that the roles of the Parties are reversed; provided, in each case ((i) or (ii)), that the Section 7.2(d)(i) language "After the Transfer Date" shall be deemed to read "On or after the effective date of termination"); 7.4; 7.5 (solely with respect to any surviving rights and obligations under the Sections cited therein); 7.6(c)(i) and (ii) (solely with respect to (i) Joint Patents and (ii) GBT Sole Patents and Other Royalty Patents as if such Patent Rights were Joint Patents; provided, in each case ((i) or (ii)), that the Section 7.6(c)(ii) language "Prior to the Option Effective Date" shall be deemed to read "On or after the effective date of termination"); 7.6(d) (solely with respect to any surviving rights and obligations under the Sections cited therein); 8.4; 10.1 through 10.3 (only until the [***] of the effective date of termination and subject to Sections 11.3(c) and (d) and provided that in the case of clause 11.3(g) the proviso shall not apply to Syros after the effective date of termination); 10.6(a); 11.3(a); 11.3(b) (solely in the termination circumstances provided therein); 11.3(c); 11.3(d); 11.4 and this Section 11.5; and Article 9 and Article 12.

(b) Without limiting the foregoing, in the case of expiration (but not termination) of this Agreement, the following provisions shall survive: Sections 2.9 (second and third sentences only); 3.7; 6.4 (solely with respect to any milestone achieved prior to the effective

date of expiration but with respect to which GBT has not paid the corresponding milestone payment(s) as of such date); 6.5-6.6 (solely with respect to Net Sales accrued prior to the effective date of expiration); 6.7; 6.8-6.9 (for clarity, with respect to any Net Sales accrued or milestone payments accrued prior to the effective date of expiration); 6.10 (solely for the term set forth therein, and, for clarity, with respect to any Net Sales accrued or milestone payments accrued prior to the effective date of expiration); 7.1; 8.4 11.1 (second sentence) and this Section 11.5; and Article 9; Article 10 (until the [***] of the date of expiration); and Article 12.

ARTICLE 12
GENERAL PROVISIONS

12.1 Force Majeure. Neither Party shall be held liable to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in performing any obligation under this Agreement to the extent such failure or delay is caused by or results from causes beyond the reasonable control of the affected Party, potentially including embargoes, war, acts of war (whether war be declared or not), acts of terrorism, insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, fire, floods, earthquakes or other acts of God, or acts, omissions or delays in acting by any governmental authority (except to the extent such acts, omissions or delays result from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement) or unavailability of materials related to the manufacture of Collaboration Compounds or Products. The affected Party shall notify the other Party in writing of such force majeure circumstances as soon as reasonably practicable, and shall promptly undertake and continue diligently all reasonable efforts necessary to cure such force majeure circumstances or to perform its obligations in spite of the ongoing circumstances.

12.2 Rights in Bankruptcy or Insolvency. All rights and licenses granted under or pursuant to this Agreement by one Party to the other Party are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that Syros or GBT (as the case may be), as licensee of intellectual property under this Agreement, shall retain and may fully exercise all of its rights and elections under the U.S. Bankruptcy Code. The Parties further agree that in the event of a rejection of this Agreement by a Party in any bankruptcy proceeding by or against such Party under the U.S. Bankruptcy Code, (a) the other Party shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property that are necessary for such other Party to practice its license to such intellectual property, which, if not already in such other Party's possession, shall be promptly delivered to it upon its written request therefor, and (b) the first Party shall not interfere with such other Party's rights to such intellectual property, and shall assist and not interfere with such other Party in obtaining such intellectual property and such embodiments of such intellectual property from another entity. The term "embodiments" of intellectual property means all tangible embodiments of the intellectual property licensed hereunder to the extent of the license scope. All rights, powers and remedies provided in this Section 12.2 are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at Law or in equity (including the Bankruptcy Code) in the event of the commencement of a case under the U.S. Bankruptcy Code.

12.3 Assignment.

(a) This Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the prior written consent of the other Party. Notwithstanding the foregoing, either Party may, without consent of the other Party, assign this Agreement and its rights and obligations hereunder in whole or in part to an Affiliate of such Party, or in whole to its successor in interest in connection with the sale of all or substantially all of its shares or its assets to which this Agreement relates, or in connection with a Change of Control or merger, acquisition or similar transaction. Any attempted assignment not in accordance with this Section 12.3 shall be null and void and of no legal effect. Any permitted assignee shall assume all assigned obligations of its assignor under this Agreement. The terms and conditions of this Agreement shall be binding upon, and shall inure to the benefit of, the Parties and their respected successors and permitted assigns.

(b) Whether or not this Agreement is assigned pursuant to Section 12.3(a), the Parties agree as follows: the rights to information, inventions, materials, Patent Rights, Know-How or other intellectual property rights:

(i) controlled by a Third Party permitted assignee of a Party or any of its Affiliates that were controlled by such assignee or any of its Affiliates (and not such Party) immediately prior to such assignment (other than as a result of a license or other grant of rights, covenant or assignment by such Party or its Affiliates to, or for the benefit of, such Third Party); or

(ii) controlled by a Third Party that becomes a controlling (as defined in Section 1.2) Affiliate of a Party as a result of a Change of Control of a Party, or by any affiliate of such Third Party that becomes an Affiliate of a Party as a result of such Change of Control, (A) that were controlled by such new Affiliate immediately prior to such Change of Control (other than as a result of a license or other grant of rights, covenant or assignment by such Party or its other Affiliates to, or for the benefit of, such Person) or (B) that become controlled by such new Affiliate after such Change of Control and independent of any activities under this Agreement,

in each case ((i) and (ii)) shall be automatically excluded from the rights licensed or granted to the other Party under this Agreement (any such excluded information, inventions, materials, Patent Rights, Know-How or other intellectual property rights, "**Excluded Transaction IP**"); provided in each case that if any Excluded Transaction IP of a Party's assignee or new Affiliate is used or incorporated by the assigning Party or Party that has undergone a Change of Control, as applicable, following such assignment or Change of Control, as the case may be, (x) in any activities under the Research Plan (in the case of either Party), or (y) in any Development, manufacture or Commercialization of a Licensed Compound or Product after the Option Effective Date, in the case of GBT, it shall no longer constitute Excluded Transaction IP hereunder.

12.4 Severability. If any one or more of the provisions contained in this Agreement is held invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein shall not in any way be affected or impaired thereby, unless the absence of the invalidated provision(s) adversely affects the substantive rights of the Parties. The Parties shall in such an instance use their best efforts to replace the invalid, illegal or

unenforceable provision(s) with valid, legal and enforceable provision(s) which, insofar as practical, implement the purposes of this Agreement.

12.5 Notices. All notices which are required or permitted hereunder shall be in writing and sufficient if delivered personally, sent by internationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, addressed as follows:

If to Syros:
Syros Pharmaceuticals, Inc.
35 CambridgePark Drive
Cambridge, Massachusetts 02140
Attn: Chief Business Officer

with a copy to:
Syros Pharmaceuticals, Inc.
35 CambridgePark Drive
Cambridge, Massachusetts 02140
Attn: Chief Legal Officer

If to GBT:
Global Blood Therapeutics, Inc.
171 Oyster Point Blvd, Suite 300
South San Francisco, CA 94080
Attention: Chief Legal Officer

or to such other address(es) as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith. Any such notice shall be deemed to have been given: (a) when delivered if personally delivered on a Business Day (or if delivered on a non- Business Day, then on the next Business Day); (b) on the Business Day after dispatch if sent by internationally-recognized overnight courier; or (c) on the [***] Business Day following the date of mailing, if sent by mail. All notices required or permitted to be given hereunder, and all written, electronic, oral or other communications between the Parties regarding this Agreement, shall be in the English language.

12.6 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of Delaware and the patent laws of the United States without reference to any rules of conflict of laws.

12.7 Dispute Resolution. The Parties recognize that disputes as to matters arising out of or in connection with this Agreement, including any question regarding its formation, existence, validity or termination, or either Party's rights or obligations hereunder, but excluding any dispute arising from the JSC, which will be resolved in accordance with Section 4.2 (collectively, "**Disputes**") may arise from time to time. It is the objective of the Parties to establish procedures to facilitate the resolution of such Disputes in an expedient manner by mutual cooperation and without resort to litigation. To accomplish this objective, the Parties agree to follow the procedures set forth in this Section 12.7 to resolve any such Dispute if and when it arises.

(a) **Resolution by Alliance Managers and Executive Officers**. If any Dispute arises, either Party may refer such Dispute to the Alliance Managers, who shall meet in person or by telephone within [***] after such referral to attempt in good faith to resolve such Dispute. If such matter cannot be resolved by discussion of the Alliance Managers within such [***] period (as may be extended by mutual written agreement), such Dispute shall be referred to the Executive Officers, who shall meet in person or by telephone within [***] after such referral to attempt in good faith to resolve such Dispute. If such matter cannot be resolved by discussion of the Executive Officers within such [***] period (as may be extended by mutual written agreement), such Dispute shall be resolved in accordance with the remainder of this Section 12.7. The Parties acknowledge that discussions between the Parties to resolve Disputes are settlement discussions under applicable rules of evidence and without prejudice to either Party's legal position.

(b) **AAA Arbitration**. Any Dispute that is not resolved through negotiations under Section 12.7(a) shall be finally settled by binding arbitration by three (3) arbitrators pursuant to the then-current Commercial Arbitration Rules of the American Arbitration Association, except where they conflict with this Section 12.7, in which case this Section 12.7 shall control. Each Party shall nominate one (1) neutral arbitrator and the two Party-nominated arbitrators shall nominate the third (3rd) neutral arbitrator, who shall serve as the presiding arbitrator, within [***] after the second (2nd) arbitrator's appointment. At the request of a Party, the arbitral tribunal shall have the discretion to order the disclosure of specified documents by the Parties. Such a request shall identify the document(s) with a reasonable degree of specificity and establish the relevance of the document(s) to the arbitration.

(c) **Seat; Language**. The seat, or legal place, of arbitration shall be Chicago, Illinois. The language of the arbitration shall be English.

(d) **Relief**. Except as otherwise specifically limited in this Agreement, the arbitral tribunal shall have the power to grant any remedy or relief that it deems appropriate, whether provisional or final, including injunctive relief. Each Party retains the right to apply to any court of competent jurisdiction for interim and/or conservatory measures, including pre-arbitral attachments or preliminary injunctions, and any such request shall not be deemed incompatible with, or a waiver of, this agreement to arbitrate. The arbitration award shall be final and binding on the Parties, and the Parties undertake to carry out any award without delay. Judgment on the award may be entered in any court of competent jurisdiction.

(e) **Costs**. Each Party shall bear its own legal fees. The arbitrators shall assess their costs, fees and expenses against the Party losing the arbitration unless they believe that neither Party is the clear winner, in which case the arbitrators shall divide such fees, costs and expenses according to their discretion. The arbitrators, in the arbitrators' discretion, may award reimbursement of attorney's fees to the prevailing Party.

(f) **Confidentiality**. The existence and content of the arbitral proceeding, including any rulings or award, shall be kept confidential by the Parties and the arbitrator except to the extent (i) required by applicable Law; (ii) required to protect or pursue a legal right; (iii) required to enforce or challenge an award; or (iv) approved by written consent of the Parties. Notwithstanding anything to the contrary herein, either Party may disclose matters relating to the

arbitration or the arbitral proceedings where necessary for the preparation or presentation of a claim or defense in such arbitration. The arbitrators shall issue appropriate protective orders to safeguard each Party's Confidential Information.

(g) **Timing**. The award shall be rendered within [***] of the appointment of the arbitral tribunal, unless the Parties jointly request an extension or the arbitral tribunal determines, in a reasoned decision, that the interest of justice or the complexity of the case requires that such limit be extended.

(h) **Survivability**. Any duty to arbitrate under this Agreement shall remain in effect and be enforceable after termination of this Agreement for any reason.

(i) **Patent and Trademark Disputes**. Any dispute, controversy or claim relating to the ownership, inventorship, scope, validity, enforceability or infringement of any patents or trademarks shall be submitted to a court of competent jurisdiction in the country in which such patent or trademark rights were granted or arose.

12.8 Entire Agreement; Amendments. This Agreement, together with the Exhibits hereto, contains the entire understanding of the Parties with respect to the subject matter hereof. Any other express or implied agreements and understandings, negotiations, writings and commitments, either oral or written, with respect to the subject matter hereof are superseded by the terms of this Agreement. The Exhibits to this Agreement are incorporated herein by reference and shall be deemed a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by authorized representative(s) of both Parties hereto. The Parties agree that, effective as of the Effective Date, the Confidentiality Agreement shall be terminated, and that disclosures made prior to the Effective Date pursuant to the Confidentiality Agreement shall after the Effective Date be subject to the confidentiality and non-use provisions of this Agreement.

12.9 Headings. The captions to the several Articles, Sections and subsections hereof are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several Articles and Sections hereof.

12.10 Independent Contractors. It is expressly agreed that Syros and GBT shall be independent contractors and that the relationship between the two Parties shall not constitute a partnership, joint venture or agency. Neither Syros nor GBT shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other Party, without the prior written consent of the other Party.

12.11 Waiver. The waiver by either Party hereto of any right hereunder, or of any failure of the other Party to perform, or of any breach by the other Party, shall not be deemed a waiver of any other right hereunder or of any other breach by or failure of such other Party whether of a similar nature or otherwise.

12.12 Cumulative Remedies. No remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

12.13 Performance by Affiliates. Each Party may discharge any obligations and exercise any right hereunder through any of its Affiliates. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance.

12.14 Limitation of Liability. NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, PUNITIVE, OR INDIRECT DAMAGES ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES. NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 12.14 IS INTENDED TO OR SHALL LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF ANY PARTY UNDER SECTION 9.1 OR 9.2, OR DAMAGES AVAILABLE FOR BREACH OF SECTION 3.6 OR ARTICLE 10.

12.15 Waiver of Rule of Construction. Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement shall be construed against the drafting Party shall not apply.

12.16 Business Day Requirements. In the event that any notice or other action or omission is required to be taken by a Party under this Agreement on a day that is not a Business Day then such notice or other action or omission shall be deemed to be required to be taken on the next occurring Business Day.

12.17 Counterparts. This Agreement may be executed in two or more counterparts by original signature, facsimile or PDF files, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

{Remainder of page intentionally left blank}

IN WITNESS WHEREOF, the Parties intending to be bound have caused this License and Collaboration Agreement to be executed by their duly authorized representatives as of the Effective Date.

Syros Pharmaceuticals, Inc.	**Global Blood Therapeutics, Inc.**
By: /s/ Nancy Simonian	By: /s/ Ted W. Love
Name: Nancy Simonian, MD	Name: Ted W. Love
Title: President & CEO	Title: CEO

List of Exhibits

Exhibit A	Initial Research Plan and Research Budget
Exhibit B	Joint Press Release
Exhibit C	Collaboration Targets
Exhibit D	Scheduled Patent
Exhibit E	List of Approved Subcontractors

{SIGNATURE PAGE TO LICENSE AND COLLABORATION AGREEMENT}

Exhibit A
Initial Research Plan and Research Budget

[***]

Exhibit B
Joint Press Release

GBT and Syros Partner to Discover, Develop and Commercialize Novel Therapies for Sickle Cell Disease and Beta Thalassemia

Collaboration Combines GBT's Therapeutic Area Leadership with Power of Syros' Gene Control Platform to Find New Medicines to Induce Fetal Hemoglobin

Syros to Receive $20 Million Upfront, Three Years of Preclinical Research Funding and Milestone Payments

SOUTH SAN FRANCISCO, Calif. and CAMBRIDGE, Mass – December 18, 2019 – Global Blood Therapeutics, Inc. (GBT) (NASDAQ: GBT) and Syros Pharmaceuticals, Inc. (NASDAQ: SYRS) today announced that they have entered into a collaboration to discover, develop and commercialize novel therapies for sickle cell disease (SCD) and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that induce fetal hemoglobin, and GBT will receive an option to obtain an exclusive worldwide license to develop, manufacture and commercialize products resulting from the collaboration.

"The discovery and development of novel therapeutic approaches to treat sickle cell disease has been a driving force for GBT since we were founded," said Ted W. Love, M.D., president and CEO of GBT. "We believe that Syros' approach to inducing fetal hemoglobin is one of the most promising ways to identify the next generation of therapies to treat sickle cell disease and beta thalassemia at a fundamental level – upstream of serious complications like organ damage, organ failure and early death. We will continue to seek the best scientific approaches to transform the treatment of these devastating lifelong diseases."

Using its gene control platform to elucidate mechanisms controlling gamma globin gene expression, Syros identified components of LRF (leukemia/lymphoma-related factor) and the NuRD (nucleosome remodeling and histone deacetylation) complex that could serve as potential targets to switch on the gamma globin gene, which is normally silenced a few months after birth. By turning on gamma globin expression, GBT and Syros aim to induce the production of fetal hemoglobin, which is known to exert protective effects on the red blood cells of sickle cell disease and beta thalassemia patients and mitigate the clinical manifestation of these diseases.

"We believe it is possible to provide a functional cure for patients with sickle cell disease or beta thalassemia by switching on the gamma globin gene with an oral medicine," said Nancy Simonian, M.D., CEO of Syros. "Partnering with GBT, an established leader in sickle cell with proven research, development, manufacturing, and commercialization capabilities, allows us to expand and accelerate our program, exploring multiple approaches in parallel with the aim of bringing much-needed new therapies to market for sickle cell and beta thalassemia patients as quickly as possible."

Syros' drug discovery program in SCD was highlighted recently in an oral presentation at the 61st American Society of Hematology (ASH) Annual Meeting, as well as in an ASH press briefing. In that presentation, Syros described its discovery of a fetal hemoglobin repressor that, when knocked down in primary cells and an erythroid cell line expressing adult hemoglobin, induced fetal hemoglobin in nearly 100% of cells and increased total fetal hemoglobin levels to 40%, exceeding levels that are associated with a functional cure in SCD patients.

Terms of the Agreement

Under the terms of the agreement, GBT will pay Syros $20 million upfront and fund up to $40 million in preclinical research for at least three years. Should GBT exercise its option under the agreement, Syros could receive up to $315 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration. Syros would also receive mid- to high-single digit royalties on sales of products resulting from the collaboration. In addition, Syros would have the option to co-promote the first product resulting from the collaboration in the United States.

About GBT

GBT is a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. Founded in 2011, GBT is delivering on its goal to transform the treatment and care of sickle cell disease (SCD), a lifelong, devasting inherited blood disorder. The company has introduced Oxbryta™ (voxelotor), the first FDA-approved treatment that directly inhibits sickle hemoglobin polymerization, the root cause of SCD. GBT is also advancing its pipeline program in SCD with inclacumab, a p-selectin inhibitor in development to address pain crises associated with the disease. In addition, GBT's drug discovery teams are working on new targets to develop the next generation of treatments for SCD. To learn more, please visit www.gbt.com and follow the company on Twitter @GBT_news.

About Syros Pharmaceuticals

Syros is redefining the power of small molecules to control the expression of genes. Based on its unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is advancing a robust pipeline of development candidates, including SY-1425, a first-in-class oral selective RARα agonist in a Phase 2 trial in a genomically defined subset of acute myeloid leukemia patients, and SY-5609, a highly selective and potent oral CDK7 inhibitor in investigational new drug application-enabling studies in cancer. Syros also has multiple preclinical and discovery programs in oncology and monogenic diseases, including sickle cell disease. For more information, visit www.syros.com and follow us on Twitter (@SyrosPharma) and LinkedIn.

Forward-Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995, including statements containing the words "will," "anticipates," "plans," "believes," "forecast," "estimates," "expects," and "intends," or similar expressions. These forward-looking statements are based on the current expectations of GBT and Syros, and actual results could differ materially. Statements in this press release may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. GBT and Syros each intend these forward-looking statements, including statements regarding the ability of the parties to discover, develop and commercialize novel therapies for SCD and beta thalassemia under the collaboration, the scientific and therapeutic potential of Syros' gene control platform and approach to inducing fetal hemoglobin, the exercise by GBT of its option under the collaboration agreement, the potential milestone payments and royalties due to Syros under the collaboration agreement and Syros' option to co-promote the first product resulting from the collaboration in the United States, to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act, and GBT and Syros make this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect the current views of GBT and Syros about their respective plans, intentions, expectations, strategies and prospects, which are based on the information currently available to the companies and on assumptions the companies have made. Neither GBT nor Syros can give any assurance that the plans, intentions, expectations or strategies will be attained or achieved, and, furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond the control of GBT and Syros including, without limitation, the timing and progress of, and any data generated from, the parties' research and development activities under the collaboration, and the amount and timing of resources devoted by each of the parties to activities under the collaboration, along with those risks set forth in GBT and Syros' respective Annual Reports on Form 10-K for the fiscal year ended December 31, 2018 and most recent Quarterly Reports on Form 10-Q filed with the U.S. Securities and Exchange Commission, as well as discussions of potential risks, uncertainties and other important factors in the companies' subsequent filings with the U.S. Securities and Exchange Commission. Except as required by law, neither GBT nor Syros assumes any obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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Exhibit C
Collaboration Targets

Gene Symbol	Approved name	ENSEMBL ID
ZBTB7a	leukemia/lymphoma-related factor	ENSG00000178951
NFIX	Nuclear Factor I X	ENSG00000008441
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
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[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

Exhibit D
Scheduled Patents

[***]

Exhibit E

Approved Subcontractors of Syros

[***]

Exhibit 10.21

CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED. SUCH EXCLUDED INFORMATION HAS BEEN MARKED WITH "[***]".

LOAN AGREEMENT

Dated as of December 17, 2019

among

GLOBAL BLOOD THERAPEUTICS, INC.

(as ***Borrower***),

BIOPHARMA CREDIT PLC

(as ***Collateral Agent*** and a ***Lender***)

and

BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP

(as a ***Lender***)

LOAN AGREEMENT

THIS LOAN AGREEMENT (this "**Agreement**"), dated as of December 17, 2019 (the "**Effective Date**") by and among GLOBAL BLOOD THERAPEUTICS, INC., a Delaware corporation (as "**Borrower**") and BIOPHARMA CREDIT PLC, a public limited company incorporated under the laws of England and Wales (as the "**Collateral Agent**" and a "**Lender**") and BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP, a Cayman Islands exempted limited partnership (as a "**Lender**"), provides the terms on which each Lender shall make, and Borrower shall repay, the Credit Extensions (as hereinafter defined). The parties hereto agree as follows:

1 ACCOUNTING AND OTHER TERMS

Except as otherwise expressly provided herein, all accounting terms not otherwise defined in this Agreement shall have the meanings assigned to them in conformity with Applicable Accounting Standards. Calculations and determinations must be made following Applicable Accounting Standards. If at any time any change in Applicable Accounting Standards would affect the computation of any financial requirement set forth in any Loan Document, and either Borrower or the Collateral Agent shall so request, the Collateral Agent and Borrower shall negotiate in good faith to amend such requirement to preserve the original intent thereof in light of such change in Applicable Accounting Standards; provided, that, until so amended, such requirement shall continue to be computed in accordance with Applicable Accounting Standards prior to such change therein. Without limiting the foregoing, leases shall continue to be classified on a basis consistent with that reflected in the audited consolidated financial statements of Borrower for the fiscal year ended December 31, 2018 for all purposes of this Agreement, notwithstanding any change in Applicable Accounting Standards relating thereto or the application thereof, unless Borrower and the Collateral Agent shall enter into a mutually acceptable amendment addressing such changes, as provided for above. Capitalized terms not otherwise defined in this Agreement shall have the meanings set forth in Section 13. All other terms contained in this Agreement, unless otherwise indicated, shall have the meaning provided by the Code to the extent such terms are defined therein. All references to "Dollars" or "$" are United States Dollars, unless otherwise noted.

For purposes of determining compliance with Section 6 with respect to the amount of any Indebtedness in a currency other than Dollars, no Default or Event of Default shall be deemed to have occurred solely as a result of changes in rates of currency exchange occurring after the time such Indebtedness is incurred, made or acquired (so long as such Indebtedness, at the time incurred, made or acquired, was permitted hereunder).

2 LOANS AND TERMS OF PAYMENT

2.1. Promise to Pay.

Borrower hereby unconditionally promises to pay Lenders the outstanding principal amount of the Term Loans advanced to Borrower by Lenders and accrued and unpaid interest thereon and any other amounts due hereunder as and when due in accordance with this Agreement.

2.2. Term Loans.

(a) Availability. Subject to the terms and conditions of this Agreement (including Sections 3.1, 3.2, 3.3 and 3.5):

(i) Each Lender severally agrees to make a term loan to Borrower on the Tranche A Closing Date in an original principal amount equal to such Lender's Tranche A Loan Commitment (collectively, the "**Tranche A Loan**"); and

(ii) Each Lender severally agrees to make a term loan to Borrower on the Tranche B Closing Date in an original principal amount equal to such Lender's Tranche B Loan Commitment (collectively, the "**Tranche B Loan**").

After repayment or prepayment (in whole or in part), no Term Loan (or any portion thereof) may be re-borrowed.

(b) Repayment.

(i) With respect to each applicable Term Loan, Borrower shall make equal quarterly payments of principal of such Term Loan commencing on the first Payment Date on or immediately following the 39th-month anniversary of the Tranche A Closing Date and continuing through the Term Loan Maturity Date; provided, that if any such day is not a Business Day, the applicable payment shall be due and payable on the first Business Day immediately after such Payment Date.

(ii) All unpaid principal with respect to the Term Loans (and, for the avoidance of doubt, all accrued and unpaid interest, all due and unpaid Lender Expenses and any and all other amounts payable under the Loan Documents) is due and payable in full on the Term Loan Maturity Date. The Term Loans may be prepaid only in accordance with Section 2.2(c), except as provided in Section 8.1.

(c) Prepayment of Term Loans.

(i) Borrower shall have the option, at any time after the Closing Date, to prepay, in whole or in part (in multiples of not less than $20,000,000 or such lesser amount as may then be outstanding), the Term Loans advanced by Lenders under this Agreement; provided that (A) Borrower provides written notice to the Collateral Agent of its election (which shall be irrevocable unless the Collateral Agent otherwise consents in writing) to prepay all or the applicable portion of the Term Loans, which notice shall include the amount of the Term Loans to be prepaid (or such remaining outstanding portion thereof) at least five (5) Business Days prior to such prepayment, and (B) such prepayment shall be accompanied by any and all accrued and unpaid interest on the aggregate principal amount to be prepaid to the date of prepayment and any amounts payable solely with respect to the prepayment of such principal amount under this Section 2.2(c)(i) pursuant to Section 2.2(e), Section 2.2(f) and Section 2.7(b), and all other amounts payable or accrued and not yet paid under this Agreement and the other Loan Documents. The Collateral Agent will promptly notify each Lender of its receipt of such notice.

(ii) Upon a Change in Control, Borrower shall promptly, and in any event no later than ten (10) days after the consummation of such Change in Control, notify the Collateral Agent in writing of the occurrence of a Change in Control, which notice shall include reasonable detail as to the nature, timing and other circumstances of such Change in Control (such notice, a "**Change in Control Notice**"). Borrower shall prepay in full all of the Term Loans advanced by Lenders under this Agreement, no later than ten (10) Business Days after delivery to the Collateral Agent of the Change in Control Notice in an amount equal to the sum of (A) all unpaid principal and any and all accrued and unpaid interest with respect to the Term Loans (or such remaining outstanding portion thereof), and (B) any applicable amounts payable with respect to the prepayment under this Section 2.2(c)(ii) pursuant to Section 2.2(e), Section 2.2(f) and Section 2.7(b) and all other amounts payable or accrued and not yet paid under this Agreement and the other Loan Documents. The Collateral Agent will promptly notify each Lender of its receipt of the Change in Control Notice, and the amount of such Lender's Applicable Percentage of such prepayment.

(d) Prepayment Application. Any prepayment of the Term Loans pursuant to Section 2.2(c) (together with the accompanying Makewhole Amount, Prepayment Premium or Additional Consideration that is payable pursuant to Section 2.2(e), Section 2.2(f) and Section 2.7, as applicable) shall be paid to Lenders in accordance with their respective Applicable Percentages for application to the Obligations in the following order: (i) first, to due and unpaid Lender Expenses; (ii) second, to accrued and unpaid interest at the Default Rate incurred pursuant to Section 2.3(b), if any; (iii) third, without duplication of amounts paid pursuant to clause (ii) above, to accrued and unpaid interest at the Term Loan Rate; (iv) fourth, to the Additional Loan Consideration; (v) fifth, to the Prepayment Premium; (vi) sixth, to the Makewhole Amount, if applicable; (vii) seventh, to the outstanding principal amount of the Term Loans being prepaid; and (viii) eighth, in the case of a prepayment of the Term Loans in whole, to any remaining amounts then due and payable under this Agreement and the other Loan Documents.

(e) Makewhole Amount.

(i) Any prepayment of the Tranche A Loan by Borrower (A) pursuant to Section 2.2(c)(i) or Section 2.2(c)(ii), or (B) as a result of the acceleration of the maturity of the Term Loans pursuant to Section 8.1(a), in each case occurring prior to the 3rd-year anniversary of the Tranche A Closing Date shall, in any such case, be accompanied by payment of an amount equal to the Tranche A Makewhole Amount.

(ii) Any prepayment of the Tranche B Loan by Borrower (A) pursuant to Section 2.2(c)(i) or Section 2.2(c)(ii), or (B) as a result of the acceleration of the maturity of the Term Loans pursuant to Section 8.1(a), in each case occurring prior to the 3rd-year anniversary of the Tranche B Closing Date shall, in any such case, be accompanied by payment of an amount equal to the Tranche B Makewhole Amount.

(f) Prepayment Premium.

(i) Any prepayment of the Tranche A Loan by Borrower (A) pursuant to Section 2.2(c)(i) or Section 2.2(c)(ii), or (B) as a result of the acceleration of the maturity of the Term Loans pursuant to Section 8.1(a), shall, in any such case, be accompanied by payment of an amount equal to the Tranche A Prepayment Premium.

(ii) Any prepayment of the Tranche B Loan by Borrower (A) pursuant to Section 2.2(c)(i) or Section 2.2(c)(ii), or (B) as a result of the acceleration of the maturity of the Term Loans pursuant to Section 8.1(a), shall, in any such case, be accompanied by payment of an amount equal to the Tranche B Prepayment Premium.

2.3. Payment of Interest on the Credit Extensions.

(a) Interest Rate.

(i) Subject to Section 2.3(b), the principal amount outstanding under each Term Loan shall accrue interest at a per annum rate equal to the LIBOR Rate plus seven percent (7.00%) per annum (the "**Term Loan Rate**"), which interest shall be payable quarterly in arrears in accordance with this Section 2.3.

(ii) Interest shall accrue on each Term Loan commencing on, and including, the day on which such Term Loan is made, and shall accrue on such Term Loan, or any portion thereof, for the day on which such Term Loan or such portion is paid.

(b) Default Rate. In the event Borrower fails to pay any of the Obligations when due, immediately (and without notice or demand by Lender or the Collateral Agent for payment thereof) to Borrower, such past due Obligations shall bear interest at a rate per annum which is three percentage points (3.00%) above the rate that is otherwise applicable thereto (the "**Default Rate**"), and such interest shall be payable entirely in cash on demand of Lender. Payment or acceptance of the increased interest rate provided in this Section 2.3(b) is not a permitted alternative to timely payment and shall not constitute a waiver of any Event of Default or otherwise prejudice or limit any rights or remedies of Lender.

(c) 360-Day Year. Interest shall be computed on the basis of a year of 360 days and the actual number of days elapsed.

(d) Payments. Except as otherwise expressly provided herein, all loan payments and any other payments hereunder by (or on behalf of) Borrower shall be made on the date specified herein to such bank account of each Lender as such Lender (or the Collateral Agent) shall have designated in a written notice to Borrower delivered on or before the Tranche A Closing Date (which such notice may be updated by such Lender (or the Collateral Agent) from time to time after the Tranche A Closing Date). Except as otherwise expressly provided herein, interest is payable quarterly on the Interest Date of each calendar quarter. Payments of principal or interest received after 2:00 p.m. on such date are considered received at the opening of business on the next Business Day. When any payment is due on a day that is not a Business Day, such payment is due the immediately next Business Day and additional fees or interest, as applicable, shall continue to accrue until paid. All payments to be made by Borrower hereunder or under any other Loan Document, including payments of principal and interest made hereunder and pursuant to any other Loan Document, and all fees, expenses, indemnities and reimbursements, shall be made without set-off, recoupment or counterclaim, in lawful money of the United States and in immediately available funds.

(e) If at any time the Collateral Agent determines (which determination shall be conclusive absent manifest error) that (i) adequate and reasonable means do not exist for determining the rate described in clause (a) of the definition of "LIBOR Rate" and such circumstances are unlikely to be temporary or (ii) the circumstances set forth in the immediately preceding clause (i) have not arisen but the supervisor for the administrator of the three-month LIBOR Rate or a Governmental Authority having jurisdiction over Lender has made a public statement identifying a specific date after which the three-month LIBOR Rate shall no longer be used for determining interest rates for loans, then Lender and Borrower shall endeavor to establish an alternate rate of interest to the three-month LIBOR Rate that gives due consideration to the then prevailing market convention for determining a rate of interest for loans in the United States at such time, and shall enter into an amendment to this Agreement to reflect such alternate rate of interest and such other related changes to this Agreement as may be applicable.

2.4. Expenses. Borrower shall pay to or reimburse (or pay directly on behalf of) each Lender and the Collateral Agent, as applicable, all of such Person's reasonable and documented Lender Expenses incurred through and after the Effective Date, promptly after receipt of a written demand therefor by such Lender or the Collateral Agent (with, in the case of any Lender, a copy of such demand to the Collateral Agent), setting forth in reasonable detail such Person's Lender Expenses.

2.5. Requirements of Law; Increased Costs. In the event that any applicable Change in Law:

(a) Does or shall subject any Lender to any Tax of any kind whatsoever with respect to this Agreement or the Term Loans made hereunder (except, in each case, Indemnified Taxes, Taxes described in clause (b) through (d) of the definition of Excluded Taxes, and Connection Income Taxes);

(b) Does or shall impose, modify or hold applicable any reserve, capital requirement, special deposit, compulsory loan, insurance charge or similar requirements against assets held by, or deposits or other liabilities in or for the account of, advances or loans by, or other credit extended by, or any other acquisition of funds by, any Lender; or

(c) Does or shall impose on any Lender any other condition (other than Taxes); and the result of any of the foregoing is to increase the cost to such Lender (as determined by such Lender in good faith using calculation methods customary in the industry) of making, renewing or maintaining the Term Loans or to reduce any amount receivable in respect thereof or to reduce the rate of return on the capital of such Lender or any Person controlling such Lender, then, in any such case, Borrower shall promptly pay to the applicable Lender, within thirty (30) days of its receipt of the certificate described below, any additional amounts necessary to compensate such Lender for such additional cost or reduced amounts receivable or rate of return as reasonably determined by such Lender with respect to this Agreement or the Term Loans made hereunder. If any Lender becomes entitled to claim any additional amounts pursuant to this Section 2.5, it shall promptly notify Borrower in writing of the event by reason of which it has become so entitled (with a copy of such notice to the Collateral Agent), and a certificate as to any additional amounts payable pursuant to the foregoing sentence containing the calculation thereof in reasonable detail submitted by such Lender to Borrower (with a copy of such certificate to the Collateral Agent) shall be conclusive in the absence of manifest error. The provisions hereof shall survive the termination of this Agreement and the payment of the outstanding Term Loans and all other Obligations. Failure or delay on the part of any Lender to demand compensation for any increased costs or reduction in amounts received or receivable or reduction in return on capital under this Section 2.5 shall not constitute a waiver of such Lender's right to demand such compensation; provided that Borrower shall not be under any obligation to compensate such Lender under this Section 2.5 with respect to increased costs or reductions with respect to any period prior to the date that is 180 days prior to the date of the delivery of the notice required pursuant to the foregoing provisions of this paragraph; provided, further, that if the Change in Law giving rise to such increased costs or reductions is retroactive, then the 180-day period referred to above shall be extended to include the period of retroactive effect thereof.

2.6. Taxes; Withholding, Etc.

(a) All sums payable by any Credit Party hereunder and under the other Loan Documents shall (except to the extent required by Requirements of Law) be paid free and clear of, and without any deduction or withholding on account of, any Tax imposed, levied, collected, withheld or assessed by any Governmental Authority. In addition, Borrower agrees to pay, and shall indemnify and hold each Lender harmless from, Other Taxes, and as soon as practicable after the date of paying such sum, Borrower shall furnish to each Lender (as applicable, with a copy to the Collateral Agent) the original or a certified copy of a receipt evidencing payment thereof or other evidence reasonably satisfactory to the Collateral Agent of such payment and of the remittance thereof to the relevant taxing or other Governmental Authority.

(b) If any Credit Party or any other Person ("**Withholding Agent**") is required by Requirements of Law to make any deduction or withholding on account of any Tax (as determined in the good faith discretion of such Withholding Agent) from any sum paid or payable by any Credit Party to any Lender under any of the Loan Documents: (i) such Withholding Agent shall notify such Lender in writing (with a copy to the Collateral Agent) of any such requirement or any change in any such requirement promptly after such Withholding Agent becomes aware of it; (ii) such Withholding Agent shall make any such withholding or deduction; (iii) such Withholding Agent shall pay any such Tax before the date on which penalties attach thereto in accordance with Requirements of Law; (iv) if the Tax is an Indemnified Tax, the sum payable by such Withholding Agent in respect of which the relevant deduction, withholding or payment of Indemnified Tax is required shall be increased to the extent necessary to ensure that, after the making of that deduction, withholding or payment (including any deductions for Indemnified Taxes applicable to additional sums payable under this Section 2.6(b)), such Lender receives on the due date a net sum equal to what it would have received had no such deduction, withholding or payment of Indemnified Tax been required or made; and (v) as soon as practicable after paying any sum from which it is required by Requirements of Law to make any deduction or withholding, Borrower shall (or shall cause such Withholding Agent, if not Borrower, to) deliver to such Lender (with a copy to the Collateral Agent) the original or a certified copy of a receipt evidencing payment thereof or other evidence reasonably satisfactory to such Lender of such deduction, withholding or payment and of the remittance thereof to the relevant taxing or other Governmental Authority.

(c) Borrower shall indemnify each Lender for the full amount of any Indemnified Taxes (including Indemnified Taxes imposed or asserted on or attributable to amounts payable under this Section 2.6(c)) paid by such Lender and any liability (including any reasonable expenses) arising therefrom or with respect thereto whether or not such Indemnified Taxes were correctly or legally imposed or asserted by the relevant Governmental Authority. Any indemnification payment pursuant to this Section 2.6(c) shall be made to the applicable Lender within thirty (30) days from written demand therefor.

(d) Any Lender that is entitled to an exemption from or reduction of withholding Tax with respect to payments made under any Loan Document shall deliver to Borrower, at the time or times reasonably requested in writing by Borrower, such properly completed and executed documentation as will permit such payments to be made without withholding or at a reduced rate of withholding. In addition, such Lender, if reasonably requested in writing by Borrower, shall deliver such other documentation prescribed by Requirements of Law or otherwise reasonably requested by Borrower to enable Borrower to determine whether or not such Lender is subject to backup withholding or information reporting requirements. Notwithstanding anything to the contrary in the preceding two sentences, the completion, execution and submission of such documentation (other than such documentation set forth in Section 2.6(d)(i), (ii) or (iv) below) shall not be required if in such Lender's reasonable judgment such completion, execution or submission would subject such Lender to any material unreimbursed cost or expense or would materially prejudice the legal or commercial position of such Lender. For the avoidance of doubt, for the purposes of this Section 2.6(d), the term "Lender" shall include each applicable assignee thereof. Without limiting the generality of the foregoing:

(i) If any Lender is organized under the laws of the United States of America or any state thereof, such Lender shall deliver to Borrower, on or prior to, the Tranche A Closing Date and, the date on which a Lender Transfer involving such Lender occurs, as applicable, and at such other times as may be necessary in the determination of Borrower, upon request in writing by Borrower (in the reasonable exercise of its discretion), two (2) executed copies of Internal Revenue Service ("**IRS**") Form W-9 certifying that such Lender is exempt from U.S. federal backup withholding tax.

(ii) If any Lender is a Foreign Lender, such Lender shall deliver, and shall cause each applicable assignee thereof to deliver, to Borrower, on or prior to, the Tranche A Closing Date and, the date on which a Lender Transfer involving such Lender occurs, as applicable, and at such other times as may be necessary in the determination of Borrower (in the reasonable exercise of its discretion):

(1) in the case of a Foreign Lender claiming the benefits of an income tax treaty to which the United States is a party (x) with respect to payments of interest under any Loan Document, a properly completed and duly executed copy of IRS Form W-8BEN or IRS Form W-8BEN-E establishing an exemption from, or reduction of, U.S. federal withholding Tax pursuant to the "interest" article of such tax treaty and (y) with respect to any other applicable payments under any Loan Document, a properly completed and duly executed copy of IRS Form W-8BEN or IRS Form W-8BEN-E establishing an exemption from, or reduction of, U.S. federal withholding Tax pursuant to the "business profits" or "other income" article of such tax treaty;

(2) a completed and duly executed copy of IRS Form W-8ECI;

(3) to the extent that such Foreign Lender is not the beneficial owner, a properly completed and duly executed copy of IRS W-8IMY and a withholding statement, along with IRS Form W-9, W-8BEN-E, W-8BEN, W-8ECI and/or other certification documents from each beneficial owner, as applicable; provided that if the Foreign Lender is a partnership and one or more direct or indirect partners of such Foreign Lender are claiming the portfolio interest exemption, such Foreign Lender may provide a certificate referenced in Section 2.6(d)(ii)(4) below on behalf of each such direct and indirect partner; or

(4) in the case of a Foreign Lender claiming the benefits of the exemption for "portfolio interest" under Section 881(c) of the IRC, it shall provide Borrower with a properly completed and duly executed copy of IRS Form W-8BEN-E or IRS Form W-8BEN, as applicable, and a certificate reasonably satisfactory to Borrower to the effect that any interest received by such Foreign Lender is not received by a "bank" on "extension of credit made pursuant to a loan agreement entered into in the ordinary course of its trade or business" within the meaning of 881(c)(3)(A) of the IRC, a "10 percent shareholder" of Borrower within the meaning of Section 871(h)(3)(B) of the IRC, or a "controlled foreign corporation" related to Borrower as described in Section 881(c)(3)(C) of the IRC.

(iii) If any Lender is a Foreign Lender it shall, to the extent it is legally entitled to do so, deliver to Borrower (in such number of copies as shall be requested by the recipient) on or prior to the date on which such Foreign Lender becomes a party to this Agreement (and from time to time thereafter upon the reasonable request of Borrower), executed copies of any other form prescribed by applicable law as a basis for claiming exemption from or a reduction in U.S. federal withholding Tax, duly completed, together with such supplementary documentation as may be prescribed by applicable law to permit Borrower to determine the withholding or deduction required to be made.

(iv) If a payment made to any Lender under any Loan Document would be subject to U.S. federal withholding Tax imposed by FATCA if such Lender were to fail to comply with the applicable reporting requirements of FATCA (including those contained in Section 1471(b) or 1472(b) of the IRC, as applicable), such Lender shall deliver to Borrower at the time or times prescribed by law and at such time or times reasonably requested by Borrower such documentation prescribed by applicable law (including as prescribed by Section 1471(b)(3)(C)(i) of the IRC) and such additional documentation reasonably requested by Borrower as may be necessary for Borrower to comply with their obligations under FATCA and to determine that Lender has complied with its obligations under FATCA or to determine the amount to deduct and withhold from such payment. Solely for purposes of this clause (iv), "FATCA" shall include any amendments made to FATCA after the date of this Agreement.

(v) If any Lender is required to deliver any forms, statements, certificates or other evidence with respect to United States federal Tax or backup withholding matters pursuant to this Section 2.6(d), such Lender hereby agrees, from time to time after the initial delivery by such Lender of such forms, certificates or other evidence, whenever a lapse in time, change in circumstances or law, or additional guidance by a Governmental Authority renders such forms, certificates or other evidence obsolete or inaccurate in any material respect, to promptly deliver to Borrower two (2) new original copies.

(vi) Borrower shall not be required to pay any additional amount to any Lender under Section 2.6(b)(iv) if such Lender shall have failed (1) to timely deliver to Borrower the forms, certificates or other evidence referred to in this Section 2.6(d) (each of which shall be complete, accurate and duly executed), or (2) to notify Borrower of its inability to deliver any such forms, certificates or other evidence, as the case may be; provided that, if such Lender shall have satisfied the requirements of this Section 2.6(d) on the Tranche A Closing Date (or on the date such Lender initially acquires an interest in a Term Loan), nothing in this last sentence of this Section 2.6(d) shall relieve Borrower of its obligations to pay any additional amounts pursuant to this Section 2.6 in the event that, solely as a result of any change in any Requirements of Law or any change in the interpretation, administration or application thereof by any applicable Governmental Authority, such Lender is no longer legally entitled to deliver forms, certificates or other evidence at a subsequent date establishing the fact that such Lender is not subject to withholding as described herein and in the forms, certificates or other evidence initially provided by such Lender.

(e) If any party hereto determines, in its discretion exercised in good faith, that it has received a refund of any Taxes or a credit or offset for any Taxes as to which it has been indemnified pursuant to this Section 2.6 (including by the payment of additional amounts pursuant to this Section 2.6), it shall pay to the indemnifying party an amount equal to such refund, credit or offset (but only to the extent of indemnity payments made, or additional amounts paid, under this Section 2.6 with respect to the Taxes giving rise to such refund), net of all out-of-pocket expenses (including Taxes) of such indemnified party and without interest (other than any interest paid by the relevant Governmental Authority with respect to such refund). Such indemnifying party, upon the request of such indemnified party, shall repay to such indemnified party the amount paid over pursuant to this clause (e) in the event that such indemnified party is required to repay, credit or offset such refund to such Governmental Authority and the requirement to repay such refund to such Governmental Authority is not due to the indemnified party's failure to timely provide complete and accurate IRS forms and other documentation required pursuant to Section 2.6(d) or Section 2.8. Notwithstanding anything to the contrary in this clause (e), in no event will the indemnified party be required to pay any amount to an indemnifying party pursuant to this clause (e) if the payment of such amount would place the indemnified party in a less favorable net after-Tax position than the indemnified party would have been in if the indemnification payments or additional amounts giving rise to such refund had not been deducted, withheld or otherwise imposed and the indemnification payments or additional amounts with respect to such tax had never been paid. This clause (e) shall not be construed to require any indemnified party to make available its Tax returns (or any other information relating to its Taxes that it deems confidential) to the indemnifying party or any other Person.

(f) Each party's obligations under this Section 2.6 shall survive any assignment of rights by, or the replacement of, a Lender, the termination of the Term Loan Commitments and the repayment, satisfaction or discharge of all obligations under any Loan Document.

2.7. Additional Consideration.

(a) As additional consideration for the obligation of each Lender to make the Term Loans pursuant to Section 2.2, on the Tranche A Closing Date, Borrower shall pay to each Lender an amount equal to the product of (i) the sum of such Lender's Tranche A Commitment plus such Lender's Tranche B Commitment, multiplied by (ii) one and one half (1.50%) (each such product, the "**Additional Commitment Consideration**"). The Additional Commitment Consideration shall be fully earned when paid and shall not be refundable for any reason whatsoever and such Additional Commitment Consideration shall be treated as original issue discount for U.S. federal income tax purposes.

(b) As additional consideration for each Lender's having made the Term Loans pursuant to Section 3.5, on each Payment Date or the date of any prepayment of any Term Loan by Borrower (i) pursuant to Section 2.2(c)(i) or Section 2.2(c)(ii) or (ii) as a result of the acceleration of the maturity of the Term Loans pursuant to Section 8.1(a), Borrower shall pay to each Lender an amount equal to such Lender's Applicable Percentage of the product of (A) the principal amount of the Term Loan(s) being paid or prepaid, multiplied by (B) 0.02 (each such product, the "**Additional Loan Consideration**" and, together with the Additional Commitment Consideration, the "**Additional Consideration**"). The Additional Loan Consideration shall be fully earned when paid and shall not be refundable for any reason whatsoever.

2.8. Evidence of Debt; Register; Collateral Agent's Books and Records; Term Loan Notes.

(a) Evidence of Debt; Register. Notwithstanding anything herein to the contrary, Borrower hereby designates the Collateral Agent to serve as Borrower's agent solely for purposes of maintaining at all times at the Collateral Agent's principal office a "book entry system" as described in Treasury Regulations Section 5f.103-1(c)(1)(ii) that identifies each beneficial owner that is entitled to a payment of principal and stated interest on each Term Loan (the "**Register**") so that each Term Loan is at all times in "registered form" as described in IRC Treasury Regulations Section 5f.103-1(c) or Proposed Section 1.163-5(b) (or, in each case, any amended or successor version). The Collateral Agent is hereby authorized by Borrower to record in the manual or data processing records of the Collateral Agent, the date and amount of each advance and the amount of the outstanding Obligations and the date and amount of each repayment of principal and each payment of interest or otherwise on account of the Obligations. Absent manifest error, such records of the Collateral Agent shall be conclusive as to the outstanding principal amount of the total outstanding Obligations, and the payment of interest, principal and other sums due hereunder; provided, however, that the failure of the Collateral Agent to make any such record entry with respect to any payment shall not limit the obligations of Borrower under the Loan Documents. Each Term Loan: (i) shall, pursuant to this clause (a), be also registered as to both principal and any stated interest with Borrower or its agent, and (ii) may be transferred by any Lender only by (1) surrender of the old instrument and either (x) the reissuance by Borrower of the old instrument to the new Lender or (y) the issuance by Borrower of a new instrument to the new Lender, or (2) confirmation with Borrower that the right to the principal and stated interest on such Term Loan is maintained through the book entry system kept by the Collateral Agent. Each Lender, severally and not jointly with any other Lender, represents that any interest that may become due and owing under this Agreement qualifies for the portfolio interest exception from withholding on interest payments pursuant to IRC Sections 871(h) and 881(c).

(b) Term Loan Notes. Borrower shall execute and deliver to each Lender to evidence such Lender's Term Loans, (i) on the Tranche A Closing Date, the Tranche A Note and (ii) on the Tranche B Closing Date, the Tranche B Note (each, a "**Term Loan Note**").

3 CONDITIONS OF TERM LOANS

3.1. Conditions Precedent to Tranche A Loan. Each Lender's obligation to advance its Applicable Percentage of the Tranche A Loan Amount is subject to the satisfaction (or waiver in accordance with Section 11.5 hereof) of the following conditions:

(a) the Collateral Agent's and each Lender's receipt of copies of the Loan Documents (including the Tranche A Note, executed by Borrower, and the Collateral Documents but excluding any Control Agreements and any other Loan Document described in Schedule 5.14 of the Disclosure Letter to be delivered after the Tranche A Closing Date) executed and delivered by each applicable Credit Party, the Disclosure Letter, if and to the extent any update thereto is necessary between the Effective Date and the Tranche A Closing Date (provided, that in no event may the Disclosure Letter be updated in a manner that would reflect or evidence a Default or Event of Default (with or without such update)) and each other schedule to such Loan Documents (the Disclosure Letter and such other schedules to be in form and substance reasonably satisfactory to the Collateral Agent);

(b) the Collateral Agent's receipt of (i) true, correct and complete copies of the Operating Documents of each of the Credit Parties, and (ii) a Secretary's Certificate, dated the Tranche A Closing Date, certifying that the foregoing copies are true, correct and complete (such Secretary's Certificate to be in form and substance reasonably satisfactory to the Collateral Agent);

(c) without limiting the generality of clause (a) above, the Collateral Agent's receipt of the Perfection Certificate for Borrower and its Subsidiaries, in form and substance reasonably satisfactory to the Collateral Agent, if and to the extent any update thereto is necessary between the Effective Date and the Tranche A Closing Date (provided, that in no event may the Perfection Certificate be updated in a manner that would reflect or evidence a Default or an Event of Default (with or without such update));

(d) the Collateral Agent's receipt of a good standing certificate for each Credit Party (where applicable), certified by the Secretary of State (or the equivalent thereof) of the jurisdiction of incorporation or formation of such Credit Party as of a date no earlier than thirty (30) days prior to the Tranche A Closing Date;

(e) the Collateral Agent's receipt of a Secretary's Certificate with completed Borrowing Resolutions with respect to the Loan Documents and the Tranche A Loan for each Credit Party, in form and substance reasonably satisfactory to the Collateral Agent;

(f) each Credit Party shall have obtained all Governmental Approvals and all consents of other Persons, if any, in each case that are necessary in connection with the transactions contemplated by the Loan Documents and each of the foregoing shall be in full force and effect and in form and substance reasonably satisfactory to the Collateral Agent;

(g) the Collateral Agent's receipt on the Tranche A Closing Date of an opinion of Goodwin Procter LLP, counsel to all of the Credit Parties, addressed to the Collateral Agent and each Lender, in form and substance reasonably satisfactory to the Collateral Agent;

(h) the Collateral Agent's receipt of (i) evidence that any products liability and general liability insurance policies maintained regarding any Collateral are in full force and effect and (ii) appropriate evidence showing the Collateral Agent, for the benefit of Lenders and the other Secured Parties, having been named as additional insured or loss payee, as applicable (such evidence to be in form and substance reasonably satisfactory to the Collateral Agent);

(i) the Collateral Agent's receipt of all documentation and other information required by bank regulatory authorities under applicable "know-your-customer" and anti-money laundering rules and regulations, including the U.S.A. Patriot Act (Title III of Pub. L. 107-56 (signed into law October 26, 2001)) (the "**Patriot Act**");

(j) payment of the Additional Commitment Consideration concurrent with the funding of the Tranche A Loan;

(k) payment of any and all Lender Expenses then due as specified in Section 2.4 hereof concurrent with the funding of the Tranche A Loan;

(l) the Collateral Agent's receipt of a certificate, dated the Tranche A Closing Date and signed by a Responsible Officer of Borrower, confirming there is no Adverse Proceeding pending or, to the Knowledge of Borrower, threatened, that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change, except as set forth on Schedule 4.7 of the Disclosure Letter (such certificate to be in form and substance reasonably satisfactory to the Collateral Agent); and

(m) the Collateral Agent's receipt of a certificate, dated the Tranche A Closing Date and signed by a Responsible Officer of Borrower, confirming satisfaction of the conditions precedent set forth in this Section 3.1 and in Section 3.3, Section 3.4 and Section 3.5 (such certificate to be in form and substance reasonably satisfactory to the Collateral Agent).

3.2. Conditions Precedent to Tranche B Loan. Each Lender's obligation to advance its Applicable Percentage of the Tranche B Loan Amount is subject to the satisfaction (or waiver in accordance with Section 11.5 hereof) of the following conditions:

(a) each Lender's receipt of the Tranche B Note, executed by Borrower, and the Collateral Agent's and such Lender's receipt of an updated Disclosure Letter, if and to the extent any update thereto is necessary between the Tranche A Closing Date and the Tranche B Closing Date (provided, that in no event may the Disclosure Letter be updated in a manner that would reflect or evidence a Default or Event of Default (with or without such update)) (to be in form and substance reasonably satisfactory to the Collateral Agent);

(b) the Collateral Agent's receipt of an updated Perfection Certificate for Borrower and its Subsidiaries, if and to the extent any update thereto is necessary between the Tranche A Closing Date and the Tranche B Closing Date (provided, that in no event may the Perfection Certificate be updated in a manner that would reflect or evidence a Default or an Event of Default (with or without such update)) (to be in form and substance reasonably satisfactory to the Collateral Agent);

(c) The Collateral Agent's receipt of a Secretary's Certificate with completed Borrowing Resolutions with respect to the Tranche B Loan for each Credit Party, in form and substance reasonably satisfactory to the Collateral Agent;

(d) payment of any and all accrued and unpaid Lender Expenses then due as specified in Section 2.4 hereof concurrent with the funding of the Tranche B Loan;

(e) no prepayment of the Tranche A Loan has been made;

(f) the Collateral Agent's receipt of a certificate, dated the Tranche B Closing Date and signed by a Responsible Officer of Borrower, confirming there is no Adverse Proceeding pending or, to the Knowledge of Borrower, threatened, that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change, except as set forth on Schedule 4.7 of the Disclosure Letter delivered in accordance with Section 3.1(l) or, to the extent updated, clause (a) above (such certificate to be in form and substance reasonably satisfactory to the Collateral Agent); and

(g) the Collateral Agent's receipt of a certificate, dated the Tranche B Closing Date and signed by a Responsible Officer of Borrower, confirming satisfaction of the conditions precedent set forth in this Section 3.2 and in Section 3.3, Section 3.4 and Section 3.5 (such certificate to be in form and substance reasonably satisfactory to the Collateral Agent).

3.3. Additional Conditions Precedent to Term Loans. The obligation of each Lender to advance its Applicable Percentage of each Term Loan is subject to the following additional conditions precedent:

(a) the representations and warranties made by the Credit Parties in Section 4 of this Agreement and in the other Loan Documents are true and correct in all material respects, unless any such representation or warranty is stated to relate to a specific earlier date, in which case such representation or warranty shall be true and correct in all material respects as of such earlier date (it being understood that any representation or warranty that is qualified as to "materiality," "Material Adverse Change," or similar language shall be true and correct in all respects, in each case, on the Closing Date (both with and without giving effect to the Term Loans) or as of such earlier date, as applicable); and

(b) there shall not have occurred (i) any Material Adverse Change or (ii) any Default or Event of Default.

3.4. Covenant to Deliver. The Credit Parties agree to deliver to the Collateral Agent or each Lender, as applicable, each item required to be delivered to Collateral Agent or each Lender, as applicable, under this Agreement as a condition precedent to any Credit Extension; provided, however, that any such items set forth on Schedule 5.14 of the Disclosure Letter shall be delivered to the Collateral Agent within the time period prescribed therefor on such schedule. The Credit Parties expressly agree that a Credit Extension made prior to the receipt by the Collateral Agent or any Lender, as applicable, of any such item shall not constitute a waiver by the Collateral Agent or any Lender of the Credit Parties' obligation to deliver such item, and the making of any Credit Extension in the absence of any such item required to have been delivered by the date of such Credit Extension shall be in the applicable Lender's sole discretion.

3.5. Procedures for Borrowing. Subject to the prior satisfaction of all other applicable conditions to the making of each Term Loan set forth in this Agreement, to obtain any Term Loan, Borrower shall deliver to the Collateral Agent and Lenders by electronic mail or facsimile a completed Payment/Advance Request for such Term Loan executed by a Responsible Officer of Borrower (which notice shall be irrevocable on and after the date on which

such notice is given and Borrower shall be bound to make a borrowing in accordance therewith), in which case each Lender agrees to advance its Applicable Percentage of such Term Loan to Borrower on the Tranche A Closing Date or Tranche B Closing Date, as applicable, by wire transfer of same day funds in Dollars, to such account(s) in the United States as may be designated in writing to the Collateral Agent by Borrower prior to the Tranche A Closing Date or Tranche B Closing Date, as applicable; provided, however, that with respect to the Tranche B Loan, Borrower shall deliver to the Collateral Agent and Lenders by electronic mail or facsimile, at its option should it wish to obtain the Tranche B Loan, such completed Payment/Advance Request on such date that is at least ninety (90) days (or such shorter period as may be agreed to by Lenders) prior to the Tranche B Closing Date set forth in such notice; provided, further, that delivery of the Payment/Advance Request must be on or prior to June 30, 2020.

4 REPRESENTATIONS AND WARRANTIES

In order to induce each Lender and the Collateral Agent to enter into this Agreement and for each Lender to make the Credit Extensions to be made on the Closing Date, each Credit Party, jointly and severally with each other Credit Party, represents and warrants to each Lender and the Collateral Agent that the following statements are true and correct as of the Effective Date and on the Closing Date on which each Term Loan is made (both with and without giving effect to such Term Loan):

4.1. Due Organization, Power and Authority. Each of Borrower and each of its Subsidiaries (a) is duly incorporated, organized or formed, and validly existing and, where applicable, in good standing under the laws of its jurisdiction of incorporation, organization or formation identified on Schedule 4.15 of the Disclosure Letter, (b) has all requisite power and authority to (i) own, lease, license and operate its assets and properties and to carry on its business as currently conducted and (ii) execute and deliver the Loan Documents to which it is a party and to perform its obligations thereunder and otherwise carry out the transactions contemplated thereby, (c) is duly qualified and, where applicable, in good standing under the laws of each jurisdiction where its ownership, lease, license or operation of assets or properties or the conduct of its business requires such qualification, and (d) has all requisite Governmental Approvals to operate its business as currently conducted; except in each case referred to clauses (a) (other than with respect to Borrower and any other Credit Party), (b)(i), (c) or (d) above, to the extent that failure to do so could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change.

4.2. Equity Interests. All of the outstanding Equity Interests in each Subsidiary of the Borrower, the Equity Interests in which are required to be pledged pursuant to the Collateral Documents, have been duly authorized and validly issued, are fully paid and, in the case of Equity Interests representing corporate interests, are non-assessable and, on the Closing Date, all such Equity Interests owned directly by Borrower or any other Credit Party are owned free and clear of all Liens except for Permitted Liens. Schedule 4.2 of the Disclosure Letter identifies each Person, the Equity Interests in which are required to be pledged on the Closing Date pursuant to the Collateral Documents.

4.3. Authorization; No Conflict. Except as set forth on Schedule 4.3 of the Disclosure Letter, the execution, delivery and performance by each Credit Party of the Loan Documents to which it is a party, and the consummation of the transactions contemplated thereby, (a) have been duly authorized by all necessary corporate or other organizational action and (b) do not and will not (i) contravene the terms of any of such Credit Party's Operating Documents, (ii) conflict with or result in any breach or contravention of, or require any payment to be made under (A) any provision of any security issued by such Credit Party or of any agreement, instrument or other undertaking to which such Credit Party is a party or affecting such Credit Party or the assets or properties of such Credit Party or any of its Subsidiaries or (B) any order, writ, judgment, injunction, decree, determination or award of any Governmental Authority by which such Credit Party or any of its properties or assets are subject, (iii) result in the creation of any Lien (other than under the Loan Documents) or (iv) violate any Requirements of Law, except, in the cases of clauses (b)(ii) and (b)(iv) above, to the extent that such conflict, breach, contravention, payment or violation could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change.

4.4. Government Consents; Third Party Consents. Except as set forth on Schedule 4.4 of the Disclosure Letter, no Governmental Approval or other approval, consent, exemption or authorization, or other action by, or notice to, or filing with, any Governmental Authority or any other Person (including any counterparty to any Current Company IP Agreement or other Material Contract) is necessary or required in connection with (a) the execution, delivery or performance by, or enforcement against, any Credit Party of this Agreement or any other Loan Document, or for the consummation of the transactions contemplated hereby or thereby, (b) the grant by any Credit

Party of the Liens granted by it pursuant to the Collateral Documents, (c) the perfection or maintenance of the Liens created under the Collateral Documents (including the priority thereof) or (d) the exercise by the Collateral Agent or any Lender of its rights under the Loan Documents or the remedies in respect of the Collateral pursuant to the Collateral Documents, except for (i) filings necessary to perfect the Liens on the Collateral granted by the Credit Parties to the Collateral Agent for the benefit of Lenders and the other Secured Parties, (ii) the approvals, consents, exemptions, authorizations, actions, notices and filings which have been duly obtained, taken, given or made and are in full force and effect, (iii) filings under state or federal securities laws and (iv) those approvals, consents, exemptions, authorizations or other actions, notices or filings, the failure of which to obtain or make could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change.

4.5. Binding Obligation. Each Loan Document has been duly executed and delivered by each Credit Party that is a party thereto and constitutes a legal, valid and binding obligation of such Credit Party, enforceable against such Credit Party in accordance with its respective terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws relating to or limiting creditors' rights generally or by general principles of equity.

4.6. Collateral. In connection with this Agreement, each Credit Party has delivered to the Collateral Agent a completed certificate signed by such Credit Party (with respect to all Credit Parties, collectively, the "**Perfection Certificate**"). Each Credit Party, jointly and severally, represents and warrants to the Collateral Agent and each Lender that:

(a) (i) its exact legal name is that indicated on the Perfection Certificate and on the signature page hereof; (ii) it is an organization of the type and is organized in the jurisdiction set forth in the Perfection Certificate; (iii) the Perfection Certificate accurately sets forth its organizational identification number or accurately states that it has none; (iv) the Perfection Certificate accurately sets forth as of the Closing Date its place of business, or, if more than one, its chief executive office as well as its mailing address (if different than its chief executive office); (v) it (and each of its predecessors) has not, in the five (5) years prior to the Closing Date, changed its jurisdiction of formation, organizational structure or type, or any organizational number assigned by its jurisdiction; and (vi) all other information set forth on the Perfection Certificate pertaining to it and each of its Subsidiaries is accurate and complete in all material respects as of the Closing Date. If any Credit Party is not now a Registered Organization but later becomes one, it shall promptly notify the Collateral Agent of such occurrence and provide the Collateral Agent with such Credit Party's organizational identification number.

(b) (i) it has good title to, has rights in, and subject to Permitted Subsidiary Distribution Restrictions, the power to transfer each item of the Collateral upon which it purports to grant a Lien under any Collateral Document, free and clear of any and all Liens except Permitted Liens, except for such minor irregularities or defects in title as could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change and (ii) it has no deposit accounts maintained at a bank or other depository or financial institution located in the United States other than the deposit accounts described in the Perfection Certificate delivered to the Collateral Agent in connection herewith.

(c) A true, correct and complete list of each pending, registered, issued or in-licensed Patent, Copyright and Trademark that, individually or taken together with any other such Patents, Copyrights or Trademarks, is material to the business of Borrower and its Subsidiaries, taken as a whole, relating in any way to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory, and is owned or co-owned by or exclusively or non-exclusively licensed to any Credit Party or any of its Subsidiaries (collectively, the "**Current Company IP**"), including its name/title, current owner or co-owners (including ownership interest), registration, patent or application number, and registration or application date, in each jurisdiction where issued or filed in the Territory, is set forth on Schedule 4.6(c) of the Disclosure Letter. Except as set forth on Schedule 4.6(c) of the Disclosure Letter, (i) (A) each item of owned Current Company IP is valid, subsisting and enforceable and no such item of Current Company IP has lapsed, expired, been cancelled or invalidated or become abandoned or unenforceable, and (B) to the Knowledge of Borrower, no written notice has been received challenging the inventorship or ownership, or relating to any lapse, expiration, invalidation, abandonment or unenforceability, of any such item of Current Company IP, and (ii) to the Knowledge of Borrower, (A) each such item of Current Company IP which is licensed from another Person is valid, subsisting and enforceable and no such item of Current Company IP has lapsed, expired, been cancelled or invalidated, or become

abandoned or unenforceable, and (B) no written notice has been received challenging the inventorship or ownership, or relating to any lapse, expiration, invalidation, abandonment or unenforceability, of any such item of Current Company IP. To the Knowledge of Borrower, there are no published patents, patent applications, articles or prior art references that could reasonably be expected to materially adversely affect the exploitation of any Product in the Territory. Except as set forth on Schedule 4.6(c) of the Disclosure Letter, (x) each Person who has or has had any rights in or to owned Current Company IP or any trade secrets owned by any Credit Party or any of its Subsidiaries, including each inventor named on the Patents within such owned Current Company IP filed by any Credit Party or any of its Subsidiaries, and has executed an agreement assigning his, her or its entire right, title and interest in and to such owned Current Company IP and such trade secrets, and the inventions, improvements, ideas, discoveries, writings, works of authorship, information and other intellectual property embodied, described or claimed therein, to the stated owner thereof, and (y) to the Knowledge of Borrower, no such Person has any contractual or other obligation that would preclude or conflict with such assignment or the exploitation of any Product in the Territory or entitle such Person to ongoing payments.

(d) (i) Each Credit Party or any of its Subsidiaries possesses valid title to the Current Company IP for which it is listed as the owner or co-owner, as applicable, on Schedule 4.6(c) of the Disclosure Letter; and (ii) there are no Liens on any Current Company IP, other than Permitted Liens.

(e) There are no maintenance, annuity or renewal fees that are currently overdue beyond their allotted grace period for any of the Current Company IP which is owned by or exclusively licensed to any Credit Party or any of its Subsidiaries, except, in each case, that could not reasonably be expected to have a materially adverse impact on such Credit Party's or Subsidiary's rights to such Current Company IP, nor have any applications or registrations therefor lapsed or become abandoned, been cancelled or expired. There are no maintenance, annuity or renewal fees that are currently overdue beyond their allotted grace period for any of the Current Company IP which is non-exclusively licensed to any Credit Party or any of its Subsidiaries, except, in each case, that could not reasonably be expected to have a materially adverse impact on such Credit Party's or Subsidiary's rights to such Current Company IP, nor to the Knowledge of Borrower, have any applications or registrations therefor lapsed or become abandoned, been cancelled or expired.

(f) There are no unpaid fees or royalties under any Current Company IP Agreement that have become due, or are expected to become overdue. Each Current Company IP Agreement is in full force and effect and, to the Knowledge of Borrower, is legal, valid, binding, and enforceable in accordance with its respective terms, except as may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws relating to or limiting creditors' rights generally or by equitable principles relating to enforceability. Neither Borrower nor any of its Subsidiaries, as applicable, is in breach of or default under any Current Company IP Agreement to which it is a party or may otherwise be bound, and to the Knowledge of Borrower, no circumstances or grounds exist that would give rise to a claim of breach or right of rescission, termination, non-renewal, revision, or amendment of any of the Current Company IP Agreements, including the execution, delivery and performance of this Agreement and the other Loan Documents.

(g) No payments by any Credit Party or any of its Subsidiaries are due to any other Person in respect of the Current Company IP, other than pursuant to the Current Company IP Agreements and those fees payable to patent offices in connection with the prosecution and maintenance of the Current Company IP and associated attorney fees.

(h) No Credit Party or any of its Subsidiaries has undertaken or omitted to undertake any acts, and, to the Knowledge of Borrower, no circumstance or grounds exist that would invalidate or reduce, in whole or in part, the enforceability or scope of (i) the Current Company IP in any manner that could reasonably be expected to materially adversely affect the exploitation of any Product in the Territory, or (ii) in the case of Current Company IP owned or co-owned by or exclusively or non-exclusively licensed to any Credit Party or any of its Subsidiaries, except as set forth on Schedule 4.6(h) of the Disclosure Letter, such Credit Party's or Subsidiary's entitlement to own or license and exploit such Current Company IP.

(i) Except as set forth on Schedule 4.6(i) of the Disclosure Letter, to the Knowledge of Borrower, there is no product or other technology of any third party that could reasonably be expected to infringe a Patent within the Current Company IP.

(j) Except as noted on Schedule 4.6(j) of the Disclosure Letter, no Credit Party is a party to, nor is it bound by, any Restricted License.

(k) In each case where an issued Patent within the Current Company IP is owned or co-owned by any Credit Party or its Subsidiaries by assignment, the assignment has been duly recorded with the U.S. Patent and Trademark Office and all similar offices and agencies anywhere in the world in which foreign counterparts are registered, filed or issued.

(l) There are no pending or, to the Knowledge of Borrower, threatened (in writing) claims against Borrower or any of its Subsidiaries alleging (i) that any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory infringes or violates (or in the past infringed or violated) the rights of any third parties in or to any Intellectual Property ("**Third Party IP**") or constitutes a misappropriation of (or in the past constituted a misappropriation of) any Third Party IP, or (ii) that any Current Company IP is invalid or unenforceable.

(m) The manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory does not, to the Knowledge of Borrower, infringe or violate (or in the past infringed or violated) any issued or registered Third Party IP (including any issued Patent within the Third Party IP) or, to the Knowledge of Borrower, constitutes a misappropriation of (or in the past constituted a misappropriation of) any Third Party IP.

(n) To the Knowledge of Borrower, there are no settlements, covenants not to sue, consents, judgments, orders or similar obligations which: (i) restrict the rights of any Credit Party or any of its Subsidiaries to use any Intellectual Property relating to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory (in order to accommodate any Third Party IP or otherwise), or (ii) permit any third parties to use any Company IP.

(o) To the Knowledge of Borrower, (i) there is no, nor has there been any, infringement or violation by any Person of any of the Company IP or the rights therein, and (ii) there is no, nor has there been any, misappropriation by any Person of any of the Company IP or the subject matter thereof.

(p) Each Credit Party and each of its Subsidiaries has taken all commercially reasonable measures customary in the pharmaceutical industry to protect the confidentiality and value of all trade secrets owned by such Credit Party or any of its Subsidiaries or used or held for use by such Credit Party or any of its Subsidiaries, in each case relating to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory.

(q) To the Knowledge of Borrower, any Product made, used or sold under the Patents within the Current Company IP has been marked with the proper patent notice.

(r) To the Knowledge of Borrower, at the time of any shipment of any Product occurring prior to the Closing Date, the units thereof so shipped complied with their relevant specifications and were developed and manufactured in accordance with current FDA Good Manufacturing Practices, FDA Good Clinical Practices, and FDA Good Laboratory Practices.

4.7. Adverse Proceedings, Compliance with Laws. Except as set forth on Schedule 4.7 of the Disclosure Letter or advised pursuant to Section 5.2(b), there are no Adverse Proceedings pending or, to the Knowledge of Borrower, threatened in writing, at law, in equity, in arbitration or before any Governmental Authority, by or against Borrower or any of its Subsidiaries or against any of their respective assets or properties or revenues (including involving allegations of sexual harassment or misconduct by any officer of Borrower or any of its Subsidiaries) that, either individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change. Neither Borrower nor any of its Subsidiaries (a) is in violation of any Requirements of Law (including Environmental Laws) that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change, or (b) is subject to or in default with respect to any final judgments, orders, writs, injunctions, decrees, rules or regulations of any court or any federal, state, municipal or other governmental department,

commission, board, bureau, agency or instrumentality, domestic or foreign, that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change. Except as set forth on Schedule 4.7 of the Disclosure Letter or advised pursuant to Section 5.2(b), there is no pending, decided or settled opposition, interference proceeding, reissue proceeding, reexamination proceeding, *inter partes* review proceeding, post-grant review proceeding, cancellation proceeding, injunction, lawsuit, paragraph IV patent certification or lawsuit under the Hatch-Waxman Act, hearing, investigation, complaint, arbitration, mediation, demand, International Trade Commission investigation, decree, or any other dispute, disagreement, or claim, in each case alleged in writing to Borrower or any of its Subsidiaries (collectively referred to hereinafter as "**Specified Disputes**"), nor to the Knowledge of Borrower, has any such Specified Dispute been threatened in writing, in each case challenging the legality, validity, enforceability or ownership of any Current Company IP.

4.8. Exchange Act Documents; Financial Statements; Financial Condition; No Material Adverse Change; Books and Records.

(a) The documents filed by Borrower with the SEC pursuant to the Exchange Act since January 1, 2019 (the "**Exchange Act Documents**"), when they were filed with the SEC, conformed in all material respects to the requirements of the Exchange Act, and as of the time they were filed with the SEC, none of such documents contained any untrue statement of a material fact or omitted to state a material fact necessary to make the statements therein (excluding any projections and forward-looking statements, estimates, budgets and general economic or industry data of a general nature), in the light of the circumstances under which they were made, not misleading; provided, that, with respect to projected financial information, Borrower represents only that such information was prepared in good faith based upon assumptions believed to be reasonable at the time (it being understood that such projections are not a guarantee of financial performance and are subject to uncertainties and contingencies, many of which are beyond the control of Borrower or any Subsidiary, and neither Borrower nor any Subsidiary can give any assurance that such projections will be attained, that actual results may differ in a material manner from such projections and any failure to meet such projections shall not be deemed to be a breach of any representation or covenant herein);

(b) The financial statements (including the related notes thereto) of Borrower and its Subsidiaries included in the Exchange Act Documents present fairly in all material respects the consolidated financial condition of Borrower and such Subsidiaries and their consolidated results of operations as of the dates indicated and the results of their operations and the changes in their cash flows for the periods specified. Such financial statements have been prepared in conformity with Applicable Accounting Standards applied on a consistent basis throughout the periods covered thereby, except as otherwise disclosed therein and, in the case of unaudited, interim financial statements, subject to normal year-end audit adjustments and the exclusion of certain footnotes, and any supporting schedules included in the Exchange Act Documents present fairly in all material respects the information required to be stated therein;

(c) Since December 31, 2018, there has not occurred or failed to occur any change or event that has had or could reasonably be expected to have, either alone or in conjunction with any other change(s), event(s) or failure(s), a Material Adverse Change, except as has been disclosed in the Exchange Act Documents; and

(d) The Books of Borrower and each of its Subsidiaries in existence immediately prior to the Effective Date contain full, true and correct entries of all dealings and transactions in relation to its business and activities in conformity with Applicable Accounting Standards and all Requirements of Law.

4.9. Solvency. Borrower and its Subsidiaries, on a consolidated basis, are Solvent. Without limiting the generality of the foregoing, there has been no proposal made or resolution adopted by any competent corporate body for the dissolution or liquidation of Borrower, nor do any circumstances exist which may result in the dissolution or liquidation of Borrower.

4.10. Payment of Taxes. All foreign, federal and state income and other material Tax returns and reports (or extensions thereof) of each Credit Party and each of its Subsidiaries required to be filed by any of them have been timely filed and are correct in all material respects, and all material Taxes which are due and payable by any Credit Party or any of its Subsidiaries and all material assessments, fees and other governmental charges upon any Credit Party or any of its Subsidiaries and upon their respective properties, assets, income, businesses and franchises which

are due and payable have been paid when due and payable except where the validity or amount thereof is being contested in good faith by appropriate proceedings; provided that (a) the applicable Credit Party has set aside on its books adequate reserves therefor in conformity with Applicable Accounting Standards and (b) the failure to pay such Taxes, individually or in the aggregate, could not reasonably be expected to result in a Material Adverse Change.

4.11. Environmental Matters. Neither Borrower nor any of its Subsidiaries nor any of their respective Facilities or operations is subject to any outstanding written order, consent decree or settlement agreement with any Person relating to any Environmental Law, any Environmental Claim, or any Hazardous Materials Activity that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change. There are and, to the Knowledge of Borrower, have been, no conditions, occurrences, or Hazardous Materials Activities which would reasonably be expected to form the basis of an Environmental Claim against Borrower or any of its Subsidiaries that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change. To the Knowledge of Borrower, no predecessor of Borrower or any of its Subsidiaries has filed any notice under any Environmental Law indicating past or present treatment of Hazardous Materials at any Facility, which would reasonably be expected to form the basis of an Environmental Claim against Borrower or any of its Subsidiaries that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change (but, for the avoidance of doubt, Borrower has not undertaken any investigation of or made any inquiries to, or relating to, any of its or its Subsidiaries' predecessors), and neither Borrower's nor any of its Subsidiaries' operations involves the generation, transportation, treatment, storage or disposal of hazardous waste, as defined under 40 C.F.R. Parts 260 270 or any state equivalent, which would reasonably be expected to form the basis of an Environmental Claim against Borrower or any of its Subsidiaries that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change. No event or condition has occurred or is occurring with respect to any Credit Party relating to any Environmental Law, any Release of Hazardous Materials, or any Hazardous Materials Activity which, individually or in the aggregate, has resulted in, or could reasonably be expected to result in, a Material Adverse Change.

4.12. Material Contracts. After giving effect to the consummation of the transactions contemplated by this Agreement, except as described on Schedule 4.12 of the Disclosure Letter, each Material Contract is a valid and binding obligation of the applicable Credit Party and, to the Knowledge of Borrower, each other party thereto, and is in full force and effect, and neither the applicable Credit Party nor, to the Knowledge of Borrower, any other party thereto is in material breach thereof or default thereunder, except where such breach or default (which default has not been cured or waived) could not reasonably be expected to give rise to any cancellation, termination or acceleration right of the applicable counterparty thereto or result in the invalidation thereof. No Credit Party or any of its Subsidiaries has received any written notice from any party thereto asserting or, to the Knowledge of Borrower threatening to assert, circumstances that could reasonably be expected to result in the cancellation, termination or invalidation of any Material Contract or the acceleration of such Credit Party's or Subsidiary's obligations thereunder.

4.13. Regulatory Compliance. No Credit Party is or is required to be, or is a company "controlled" by, an "investment company" as defined in, or is subject to regulation under, the Investment Company Act of 1940. Each Credit Party has complied in all material respects with the Federal Fair Labor Standards Act. Except as could not, either individually or in the aggregate, reasonably be expected to result in a Material Adverse Change, each Plan is in compliance with the applicable provisions of ERISA, the IRC and other U.S. federal or state Requirements of Law, respectively. (i) No ERISA Event has occurred or is reasonably expected to occur; (ii) neither any Credit Party nor any ERISA Affiliate has incurred, or reasonably expects to incur, any liability (and no event has occurred which, with the giving of notice under Section 4219 of ERISA, would result in such liability) under Section 4201 *et seq*. or 4243 of ERISA with respect to a Multiemployer Plan; and (iii) neither any Credit Party nor any ERISA Affiliate has engaged in a transaction that would be subject to Section 4069 or 4212(c) of ERISA, except, with respect to each of clauses (i), (ii) and (iii) above, as could not reasonably be expected, individually or in the aggregate, to result in a Material Adverse Change.

4.14. Margin Stock. No Credit Party is engaged principally, or as one of its important activities, in extending credit for the purpose of, whether immediate or ultimate, of purchasing or carrying Margin Stock. No Credit Party owns any Margin Stock. No Credit Party or any of its Subsidiaries has taken or permitted to be taken any action that might cause any Loan Document to violate Regulation T, U or X of the Federal Reserve Board.

4.15. Subsidiaries. Schedule 4.15 of the Disclosure Letter (a) sets forth the name and jurisdiction of incorporation, organization or formation of Borrower and each of its Subsidiaries and (b) sets forth the ownership interest of Borrower and any other Credit Party in each of their respective Subsidiaries, including the percentage of such ownership.

4.16. Employee Matters. Neither Borrower nor any of its Subsidiaries is engaged in any unfair labor practice that could reasonably be expected to result in a Material Adverse Change. There is (a) no unfair labor practice complaint pending against Borrower or any of its Subsidiaries or, to the Knowledge of Borrower, threatened in writing against any of them before the National Labor Relations Board, and no grievance or arbitration proceeding arising out of or under any collective bargaining agreement that is pending against Borrower or any of its Subsidiaries or, to the Knowledge of Borrower, threatened in writing against any of them, (b) no strike or work stoppage in existence or, to the Knowledge of Borrower, threatened in writing involving Borrower or any of its Subsidiaries, and (c) to the Knowledge of Borrower, no union representation question existing with respect to the employees of Borrower or any of its Subsidiaries and, to the Knowledge of Borrower, no union organization activity that is taking place that in each case specified in any of clauses (a), (b) and (c), individually or taken together with any other matter specified in clause (a), (b) or (c), could reasonably be expected to result in a Material Adverse Change.

4.17. Full Disclosure. None of the documents, certificates or written statements (excluding any projections and forward-looking statements, estimates, budgets and general economic or industry data of a general nature) furnished or otherwise made available to the Collateral Agent or any Lender by or on behalf of any Credit Party for use in connection with the transactions contemplated hereby (in each case, taken as a whole and as modified or supplemented by other information so furnished promptly after the same becomes available) contains any untrue statement of a material fact or omits to state a material fact necessary in order to make the statements contained herein or therein, as of the time when made or delivered, not misleading in light of the circumstances in which the same were made; provided, that, with respect to projected financial information, Borrower represents only that such information was prepared in good faith based upon assumptions believed to be reasonable at the time (it being understood that such projections are not a guarantee of financial performance and are subject to uncertainties and contingencies, many of which are beyond the control of Borrower or any Subsidiary, and neither Borrower nor any Subsidiary can give any assurance that such projections will be attained, that actual results may differ in a material manner from such projections and any failure to meet such projections shall not be deemed to be a breach of any representation or covenant herein). To the Knowledge of Borrower, there are no facts (other than matters of a general economic or industry nature) that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change and that have not been disclosed herein or in such other documents, certificates and written statements furnished or made available to the Collateral Agent or any Lender for use in connection with the transactions contemplated hereby.

4.18. FCPA; Patriot Act; OFAC; **Export and Import Laws**.

(a) None of Borrower, its Subsidiaries or, to the Knowledge of Borrower, any director, officer, agent or employee of Borrower or any Subsidiary of Borrower has (i) used any corporate funds of Borrower or any of its Subsidiaries for any unlawful contribution, gift, entertainment or other unlawful expense relating to political activity, (ii) made any direct or indirect unlawful payment to any foreign or domestic government official or employee or any Person from corporate funds of Borrower or any of its Subsidiaries, (iii) violated or is in violation of any provision of the U.S. Foreign Corrupt Practices Act of 1977 (the "**FCPA**") or the U.K. Bribery Act ("**UKBA**") or (iv) made any bribe, rebate, payoff, influence payment, kickback or other unlawful payment, and no part of the proceeds of any Credit Extension will be used, directly or indirectly, for any payments to any governmental official or employee, political party, official of a political party, candidate for political office or anyone else acting in an official capacity, in order to obtain, retain or direct business, or to obtain any improper advantage, in violation of the FCPA, UKBA or any other applicable anti-corruption laws;

(b) (i) The operations of Borrower and its Subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, the Bank Secrecy Act of 1970 (as amended by Title III of the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism (USA PATRIOT) Act of 2001) and the anti-money laundering laws, rules and regulations of each jurisdiction (foreign or domestic) in which Borrower or any of its Subsidiaries is subject to such jurisdiction's Requirements of Law (collectively, the "**Anti-Money Laundering Laws**") and (ii) no action, suit or proceeding by or before any Governmental Authority or any arbitrator involving Borrower or any of its Subsidiaries with respect to the Anti-Money Laundering Laws is pending or to the Knowledge of Borrower, threatened in writing; and

(c) None of Borrower, its Subsidiaries or, to the Knowledge of Borrower, any director, officer, agent or employee of Borrower or any Subsidiary of Borrower is, or is owned or controlled by individuals or entities that are, the target or subject of any sanctions administered and enforced by the Office of Foreign Assets Control of the U.S. Department of the Treasury ("**OFAC**"), the U.S. Department of State, the United Nations Security Council, the European Union, or Her Majesty's Treasury (collectively "**Sanctions**"). Borrower will not, directly or, to the Knowledge of Borrower, indirectly through an agent, use the proceeds of the Credit Extension, or lend, contribute or otherwise make available such proceeds to any Subsidiary, joint venture partner or other Person, for the purpose of financing the activities of any Person that is the target or subject of Sanctions or in any country or territory that at the time of such funding, is the subject of Sanctions.

(d) Borrower, its Subsidiaries, and to the Knowledge of Borrower, their respective directors, officers, agents and employees, are in compliance with all applicable Sanctions. Borrower and its Subsidiaries have instituted and maintain procedures reasonably designed to ensure compliance with applicable Sanctions.

(e) Borrower and its Subsidiaries are in compliance, in all materials respects, with applicable Export and Import Laws.

4.19. Health Care Matters.

(a) *Compliance with Health Care Laws*. Except as set forth on Schedule 4.19(a) of the Disclosure Letter, each Credit Party and, to the Knowledge of Borrower, each of its Subsidiaries and each officer, Affiliate, and employee acting on behalf of such Credit Party or any of its Subsidiaries, is in compliance in all material respects with all Health Care Laws.

(b) *Compliance with FDA Laws*. Each Credit Party and, to the Knowledge of Borrower, each of its Subsidiaries, are in compliance in all material respects with all applicable FDA Laws, including the Food Drug and Cosmetic Act (21 U.S.C. § 301 et seq.) and the regulations promulgated thereunder (the "**FDCA**"), in any way relating to any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory. Any Product distributed or sold in the Territory at all times during the past five (5) years has been (i) manufactured in all material respects in accordance with current FDA Good Manufacturing Practices, FDA Good Clinical Practices and FDA Good Laboratory Practices (as applicable), and (ii) if and to the extent such Product is required to be approved or cleared by the FDA pursuant to the FDCA in order to be legally marketed in the United States for such Product's intended uses, such Product has been approved or cleared for such intended uses, and no inquiries regarding material issues have been initiated by FDA.

(c) *Applicability of DEA Laws.* The Product does not contain a controlled substance (as that term is defined under the Controlled Substances Act (21 U.S.C. § 801 et seq.)).

(d) *Material Statements*. Within the past four (4) years, neither any Credit Party, nor, to the Knowledge of Borrower, any Subsidiary or any officer, Affiliate or employee of any Credit Party or Subsidiary in its capacity as a Subsidiary or as an officer, Affiliate or employee of a Credit Party or Subsidiary (as applicable), nor, to the Knowledge of Borrower, any agent of any Credit Party or Subsidiary, (i) has made an untrue statement of a material fact or a fraudulent statement to any Governmental Authority, (ii) has failed to disclose a material fact to any Governmental Authority, or (iii) has otherwise committed an act, made a statement or failed to make a statement that, at the time such statement or disclosure was made (or, in the case of such failure, should have been made) or such act was committed, could reasonably be expected to constitute a material violation of any Health Care Law.

(e) *Proceedings; Audits*. Except as has been disclosed in the Exchange Act Documents or as set forth on Schedule 4.19(e) of the Disclosure Letter: (i) there is no Adverse Proceeding pending or, to the Knowledge of Borrower, threatened in writing, against any Credit Party or any of its Subsidiaries relating to any allegations of non-compliance with any Health Care Laws, Data Protection Laws, or FDA Laws; and (ii) to the Knowledge of Borrower, there are no facts, circumstances or conditions that, individually or in the aggregate, would reasonably be expected to form the basis for any such Adverse Proceeding.

(f) *Safety Notices*. Neither any Credit Party nor any of its Subsidiaries has initiated or otherwise engaged in any recalls, field notifications, safety warnings, "dear doctor" letters, investigator notices, safety alerts or other notices of action, including as a result of any Risk Evaluation and Mitigation Strategy proposed or enforced by the FDA, relating to an alleged lack of safety or regulatory compliance of any Product that could reasonably be expected to result in a Material Adverse Change. Neither any Credit Party nor any of its Subsidiaries has a reasonable expectation that there are grounds for imposition of a clinical hold, as described in 21 C.F.R. § 312.42.

(g) *Prohibited Transactions; No Whistleblowers*. Within the past six (6) years, to the Knowledge of Borrower, neither any Credit Party, any Subsidiary, any of officer, Affiliate or employee of a Credit Party or Subsidiary, nor any other Person acting on behalf of any Credit Party or any Subsidiary, directly or indirectly: (i) has offered or paid any remuneration, in cash or in kind, to, or made any financial arrangements with, any past, present or potential patient, supplier, physician or contractor, in order to illegally obtain business or payments from such Person in material violation of any Health Care Law; (ii) has given or made, or is party to any illegal agreement to give or make, any illegal gift or gratuitous payment of any kind, nature or description (whether in money, property or services) to any past, present or potential patient, supplier, physician or contractor, or any other Person in material violation of any Health Care Law; (iii) has given or made, or is party to any agreement to give or make on behalf of any Credit Party or any of its Subsidiaries, any contribution, payment or gift of funds or property to, or for the private use of, any governmental official, employee or agent where either the contribution, payment or gift or the purpose of such contribution, payment or gift is or was a material violation of the laws of any Governmental Authority having jurisdiction over such payment, contribution or gift; (iv) has established or maintained any unrecorded fund or asset for any purpose or made any materially misleading, false or artificial entries on any of its books or records for any reason; or (v) has made, or is party to any agreement to make, any payment to any Person with the intention or understanding that any part of such payment would be in material violation of any Health Care Law. To the Knowledge of Borrower, there are no actions pending or threatened (in writing) against any Credit Party or any of its Subsidiaries or any of their respective Affiliates under any foreign, federal or state whistleblower statute, including under the False Claims Act of 1863 (31 U.S.C. § 3729 et seq.).

(h) *Exclusion*. Neither any Credit Party nor, to the Knowledge of Borrower, any Subsidiary or any officer, Affiliate or employee having authority to act on behalf of any Credit Party or any Subsidiary, is or, to the Knowledge of Borrower, has been threatened in writing to be: (i) excluded from any Governmental Payor Program pursuant to 42 U.S.C. § 1320a-7b and related regulations; (ii) "suspended" or "debarred" from selling any products to the U.S. government or its agencies pursuant to the Federal Acquisition Regulation relating to debarment and suspension applicable to federal government agencies generally (42 C.F.R. Subpart 9.4), or other U.S. Requirements of Law; (iii) debarred, disqualified, suspended or excluded from participation in Medicare, Medicaid or any other Governmental Payor Program or is listed on the General Services Administration list of excluded parties; or (iv) a party to any other action or proceeding by any Governmental Authority that would prohibit the applicable Credit Party or Subsidiary from distributing or selling any Product in the Territory or providing any services to any governmental or other purchaser pursuant to any Health Care Laws.

(i) *HIPAA*. Each Credit Party and, to the Knowledge of Borrower, each of its Subsidiaries, to the extent applicable, is in material compliance with all applicable foreign, federal, state and local laws and regulations regarding the privacy, data protection, security, and notification of breaches of health information and regarding electronic transactions, including HIPAA and GDPR, and each Credit Party and, to the Knowledge of Borrower, each of its Subsidiaries, to the extent applicable, has implemented policies, procedures and training customary in the pharmaceutical industry or otherwise adequate to assure continued compliance and to detect non-compliance. No Credit Party is a "covered entity" as defined in 45 C.F.R. § 160.103, and no Credit Party or any Subsidiary is required to comply with the General Data Protection Regulation (EU 2016/279) ("**GDPR**").

(j) *Corporate Integrity Agreement*. Neither any Credit Party or Subsidiary, nor any of their respective Affiliates, nor any officer, director, managing employee or, to the Knowledge of Borrower, agent (as those terms are defined in 42 C.F.R. § 1001.1001) of any Credit Party or Subsidiary, is a party or is otherwise subject to any order, individual integrity agreement, or corporate integrity agreement with any U.S. Governmental Authority concerning compliance with any laws, rules, or regulations, issued under or in connection with a Governmental Payor Program.

4.20. Regulatory Approvals.

(a) Except as set forth on Schedule 4.20(a) of the Disclosure Letter, each Credit Party and each Subsidiary involved in any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory has all Regulatory Approvals material to the conduct of its business and operations.

(b) Each Credit Party, each Subsidiary and, to the Knowledge of Borrower, each licensee of a Credit Party or a Subsidiary of any Intellectual Property relating to any Product, is in compliance with, and at all times during the past four (4) years, has complied with, all applicable, federal, state and local laws, rules and regulations governing the research, development, manufacture, production, use, commercialization, marketing, importing, distribution or sale of any Product in the Territory, including all such regulations promulgated by each applicable Regulatory Agency (including the FDA), except where any instance of failure to comply with any such laws, rules or regulations could not, whether individually or taken together with any other such failures, reasonably be expected to result in a Material Adverse Change. No Credit Party or its Subsidiaries has received any written notice from any Regulatory Agency citing action or inaction by any Credit Party or any of its Subsidiaries that would constitute a violation of any applicable foreign, federal, state or local laws, rules, or regulations, including a Warning Letter or Untitled Letter from FDA, which could reasonably be expected to result in a Material Adverse Change.

4.21. Supply and Manufacturing.

(a) Except as set forth on Schedule 4.21(a) of the Disclosure Letter, to the Knowledge of Borrower, the Product at all times has been manufactured in sufficient quantities and of a sufficient quality to satisfy demand of the Product during its clinical trials, without the occurrence of any event causing inventory of the Product to have become exhausted prior to satisfying such demand. To the Knowledge of Borrower, at all times following the approval of the Product by the FDA for any indication in the United States, no event has occurred that has caused or could reasonably be expected to cause (i) the Product to be manufactured in a quantity or of a quality insufficient to satisfy current or future demand of the Product in the United States for such indication or (ii) inventory of the Product in the United States for such indication to have become exhausted prior to satisfying such demand.

(b) Except as disclosed in the Exchange Act Documents or set forth on Schedule 4.21(b) of the Disclosure Letter, to the Knowledge of Borrower, (i) no manufacturer of any Product has received in the past five (5) years a Form 483 or is currently subject to a Form 483 impacting any Product with respect to any facility in the Territory manufacturing any Product, and (ii) with respect to each such Form 483 received (if any), all scientific and technical violations or other issues relating to good manufacturing practice requirements documented therein, and any disputes regarding any such violations or issues, have been corrected or otherwise resolved.

(c) Except as disclosed in Schedule 4.21(c), no Credit Party or any of its Subsidiaries has received any notice, oral or written, from any party to any Manufacturing Agreement containing any indication by or intent or threat of, such party to reduce or cease, in any material respect, the supply of Product or the active pharmaceutical ingredient incorporated therein in the Territory through calendar year 2025 (or such earlier date in accordance with the terms and conditions of such Manufacturing Agreement, as applicable).

4.22. Cybersecurity and Data Protection.

(a) Except as set forth in Schedule 4.22(a) of the Disclosure Letter, the information technology systems used in the business of Borrower and its Subsidiaries operate and perform in all material respects as required to permit Borrower and its Subsidiaries to conduct their business as presently conducted. Except as set forth on Schedule 4.22(a) of the Disclosure Letter, Borrower and its Subsidiaries have implemented and maintain a commercially reasonable enterprise-wide privacy and information security program with plans, policies and procedures for privacy, physical and cyber security, disaster recovery, business continuity and incident response, including reasonable and appropriate administrative, technical and physical safeguards to protect information subject

to Data Protection Laws as well as information and other materials in which Borrower or any of its Subsidiaries have Intellectual Property rights (including Company IP) or nondisclosure obligations, and the information technology systems of Borrower and each of its Subsidiaries, from any unauthorized access, use, control, disclosure, destruction or modification. Except as set forth on Schedule 4.22(a) of the Disclosure Letter, neither Borrower nor any of its Subsidiaries, nor to the Knowledge of Borrower, any vendor of Borrower or any of its Subsidiaries, has suffered any data breaches or other incidents that have resulted in such unauthorized access, acquisition, use, control, disclosure, destruction, or modification of any information subject to Data Protection Laws, any information or other materials subject to non-disclosure obligations or any material Company IP, or have resulted in such unauthorized access to, control of, or disruption of the information technology systems of Borrower or any of its Subsidiaries, as could have a material adverse effect on the Company and its Subsidiaries as a whole. Borrower and each of its Subsidiaries is in material compliance with the requirements of (A) their respective enterprise-wide privacy and information security programs, (B) Data Protection Laws, (C) all Material Contracts regarding the privacy and security of customer, consumer, patient, clinical trial participant, employee and other personal data, (D) their respective contractual non-disclosure obligations and (E) their respective published privacy policies. In the past six (6) years, there have not been any third party claims related to, any loss, theft, unauthorized access to, or unauthorized acquisition, modification, disclosure, corruption, destruction, or other misuse of any information subject to Data Protection Laws (including any ransomware incident) that Borrower or any of its Subsidiaries creates, receives, maintains, or transmits.

(b) In the past six (6) years, neither Borrower nor any of its Subsidiaries has received any written notice of any claims, investigations (including investigations by any Governmental Authority), or alleged violations relating to any information subject to Data Protection Laws created, received, maintained or transmitted by Borrower or any of its Subsidiaries.

4.23. Additional Representations and Warranties.

(a) After giving effect to consummation of the transactions contemplated by this Agreement, there is no Indebtedness other than Permitted Indebtedness described in clauses (a) and (b) of the definition of "Permitted Indebtedness".

(b) There are no Hedging Agreements.

(c) Except as has been disclosed in the Exchange Act Documents, there is no registration rights agreement, investors' rights agreement or other similar agreement relating to, governing or otherwise affecting the ownership of the capital stock or other equity ownership interests of any Credit Party.

5 AFFIRMATIVE COVENANTS

Each Credit Party covenants and agrees that, until payment in full of all Obligations (other than inchoate indemnity obligations), each Credit Party shall, and shall cause each of its Subsidiaries to:

5.1. Maintenance of Existence. (a) Preserve, renew and maintain in full force and effect its and all its Subsidiaries' legal existence under the Requirements of Law in their respective jurisdictions of organization, incorporation or formation; (b) take all commercially reasonable action to maintain all rights, privileges (including its good standing), permits, licenses and franchises necessary or desirable for it and all of its Subsidiaries in the ordinary course of its business, except in the case of clause (a) (other than with respect to Borrower) and clause (b) above, (i) to the extent that failure to do so could not reasonably be expected to result in a Material Adverse Change or (ii) pursuant to a transaction permitted by this Agreement; and (c) comply with all Requirements of Law of any Governmental Authority to which it is subject, except where the failure to do so could not reasonably be expected to result, individually or in the aggregate, in a Material Adverse Change.

5.2. Financial Statements, Notices. Deliver to the Collateral Agent:

(a) Financial Statements.

(i) Annual Financial Statements. As soon as available, but in any event within ninety (90) days after the end of each fiscal year of Borrower (or such earlier date on which Borrower is required to file a Form 10-K under the Exchange Act, as applicable), beginning with the fiscal year ending December 31, 2019, a consolidated balance sheet of Borrower and its Subsidiaries as of the end of such fiscal year, and the related consolidated statements of income, cash flows and stockholders' equity for such fiscal year, setting forth in each case in comparative form the figures for the previous fiscal year, all prepared in accordance with Applicable Accounting Standards, with such consolidated financial statements to be audited and accompanied by (x) a report and opinion of Borrower's independent certified public accounting firm of recognized national standing (which report and opinion shall be prepared in accordance with Applicable Accounting Standards and shall not be subject to any qualification as to "going concern" or scope of audit), stating that such financial statements fairly present, in all material respects, the consolidated financial condition, results of operations and cash flows of Borrower and its Subsidiaries as of the dates and for the periods specified in accordance with Applicable Accounting Standards, and (y) if and only if Borrower is required to comply with the internal control provisions pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 requiring an attestation report of such independent certified public accounting firm, an attestation report of such independent certified public accounting firm as to Borrower's internal controls pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 attesting to management's assessment that such internal controls meet the requirements of the Sarbanes-Oxley Act of 2002; provided, however, that Borrower shall be deemed to have made such delivery of such consolidated financial statements if such consolidated financial statements shall have been made available within the time period specified above on the SEC's EDGAR system (or any successor system adopted by the SEC);

(ii) Quarterly Financial Statements. As soon as available, but in any event within forty-five (45) days after the end of each of the first three (3) fiscal quarters of each fiscal year of Borrower (or such earlier date on which Borrower is required to file a Form 10-Q under the Exchange Act, as applicable), beginning with the fiscal quarter ending March 31, 2020, a consolidated balance sheet of Borrower and its Subsidiaries as of the end of such fiscal quarter, and the related consolidated statements of income and cash flows and for such fiscal quarter and (in respect of the second and third fiscal quarters of such fiscal year) for the then-elapsed portion of Borrower's fiscal year, setting forth in each case in comparative form the figures for the comparable period or periods in the previous fiscal year, all prepared in accordance with Applicable Accounting Standards and not subject to any qualification as to "going concern" under ASC 205-40, subject to normal year-end audit adjustments and the absence of disclosures normally made in footnotes; provided, however, that Borrower shall be deemed to have made such delivery of such consolidated financial statements if such consolidated financial statements shall have been made available within the time period specified above on the SEC's EDGAR system (or any successor system adopted by the SEC). Such consolidated financial statements shall be certified by a Responsible Officer of Borrower as, to his or her knowledge, fairly presenting, in all material respects, the consolidated financial condition, results of operations and cash flows of Borrower and its Subsidiaries as of the dates and for the periods specified in accordance with Applicable Accounting Standards consistently applied, and on a basis consistent with the audited consolidated financial statements referred to under Section 5.2(a)(i), subject to normal year-end audit adjustments and the absence of footnotes (but not, for the avoidance of doubt, subject to any qualification as to "going concern" under ASC 205-40); provided, however, that such certification by a Responsible Officer of Borrower shall be deemed to have made if a similar certification is required under the Sarbanes-Oxley Act of 2002 and such certification shall have been made available within the time period specified above on the SEC's EDGAR system (or any successor system adopted by the SEC);

(iii) Quarterly Compliance Certificate. Within five (5) Business Days, following a written request (including electronic mail) by the Collateral Agent, a duly completed Compliance Certificate signed by a Responsible Officer, certifying, among other things, that (A) such financial statements fairly present, in all material respects, the consolidated financial condition, results of operations and cash flows of Borrower and its Subsidiaries as of applicable the dates and for the applicable periods in accordance with Applicable Accounting Standards consistently applied, and are not subject to any qualification as to "going concern" under ASC 205-40, and (B) no Event of Default or Default has occurred or, if such an Event of Default or Default has occurred, specifying the nature and extent thereof and any corrective action taken or proposed to be taken with respect thereto; and

(iv) Information During Event of Default. As promptly as practicable (and in any event within five (5) Business Days of the request therefor), such additional information regarding the business or financial affairs of Borrower or any of its Subsidiaries, or compliance with the terms of this Agreement or any other Loan Documents, as the Collateral Agent may from time to time reasonably request during the existence of any Event of Default (subject to reasonable requirements of confidentiality, including requirements imposed by Requirements of Law or contract; provided that Borrower shall not be obligated to disclose any information that is reasonably subject to the assertion of attorney-client privilege or attorney work-product).

(b) Notice of Defaults or Events of Default, ERISA Events and Material Adverse Changes. Written notice as promptly as practicable (and in any event within five (5) Business Days) after a Responsible Officer of Borrower shall have obtained knowledge thereof, of the occurrence of any (i) Default or Event of Default, (ii) ERISA Event or (iii) Material Adverse Change.

(c) Legal Action Notice. Prompt written notice (which shall be deemed given to the extent reported in the Borrower's periodic or current reporting under the Exchange Act and available on the SEC's EDGAR system (or any successor system adopted by the SEC)) of any legal action, litigation, investigation or proceeding pending or threatened in writing against any Credit Party or any Subsidiary (i) that could reasonably be expected to result in uninsured damages or costs to such Credit Party or such Subsidiary in an amount in excess of the materiality thresholds applied by Borrower in accordance with the Exchange Act and related regulations and standards for purposes of its Exchange Act reporting or (ii) which alleges potential violations of the Health Care Laws, the FDA Laws or any applicable statutes, rules, regulations, standards, guidelines, policies and order administered or issued by any foreign Governmental Authority, which, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change; and in each case, provide such additional information (including any material development therein) as the Collateral Agent may reasonably request in relation thereto; provided that Borrower shall not be obligated to disclose any information that is reasonably subject to the assertion of attorney-client privilege or attorney work-product.

(d) Competing Product. If the Credit Party or any of its Subsidiaries develops or obtains rights to any approved product that is a Competing Product in the United States, or any product candidate that if approved by a Regulatory Agency would be a Competing Product in the United States at any time on or prior to the Term Loan Maturity Date, in any case, the Parties agree that the definition of "Product" will be deemed to include such Competing Product.

5.3. Taxes. Timely file all foreign, federal and state income and other material required Tax returns and reports or extensions therefor and timely pay all material foreign, federal, state and local Taxes, assessments, deposits and contributions imposed upon it or any of its properties or assets or in respect of any of its income, businesses or franchises before any penalty or fine accrue thereon; provided, however, that no such Tax or any claim for Taxes that have become due and payable and have or may become a Lien on any Collateral shall be required to be paid if (a) it is being contested in good faith by appropriate proceedings promptly instituted and diligently conducted, so long as adequate reserves therefor have been set aside on its books and maintained in conformity with Applicable Accounting Standards, and (b) solely in the case of a Tax or claim that has or may become a Lien against any Collateral, such contest proceedings conclusively operate to stay the sale or forfeiture of any portion of any Collateral to satisfy such Tax or claim. No Credit Party will, nor will it permit any of its Subsidiaries to, file or consent to the filing of any consolidated income Tax return with any Person (other than Borrower or any of its Subsidiaries) without the Collateral Agent's consent.

5.4. Insurance. Maintain with financially sound and reputable insurance companies, insurance with respect to its properties and business against loss or damage of the kinds customarily insured against by Persons of comparable size engaged in the same or similar business, of such types and in such amounts (after giving effect to any self-insurance reasonable and customary for similarly situated Persons of comparable size engaged in the same or similar businesses as Borrower and its Subsidiaries) as are customarily carried under similar circumstances by such other Persons. Any products liability or general liability insurance maintained in the United States regarding Collateral shall name the Collateral Agent, on behalf of the Lenders and the other Secured Parties, as additional insured or loss payee, as applicable (the additional insured clauses or endorsements for which, in form and substance reasonably satisfactory to the Collateral Agent). So long as no Event of Default shall have occurred and be continuing, the Borrower and its Subsidiaries may retain all or any portion of the proceeds of any insurance of the Borrower and its Subsidiaries (and each Lender shall promptly remit to the Borrower any proceeds with respect to any insurance received by it).

5.5. Operating Accounts. In the case of any Credit Party, contemporaneously with the establishment of any new Collateral Account at or with any bank or other depository or financial institution located in the United States, subject such account to a Control Agreement that is reasonably acceptable to the Collateral Agent. For each Collateral Account that each Credit Party at any time maintains, such Credit Party shall cause the applicable bank or other depository or financial institution located in the United States at or with which any Collateral Account is maintained to execute and deliver a Control Agreement or other appropriate instrument with respect to such Collateral Account to perfect the Collateral Agent's Lien, for the benefit of Lenders and the other Secured Parties, in such Collateral Account in accordance with the terms hereunder, which Control Agreement may not be terminated without the prior written consent of the Collateral Agent. The provisions of the previous two (2) sentences shall not apply to (1) accounts exclusively used for payroll, payroll Taxes and other employee wage and benefit payments to or for the benefit of any Credit Party's employees, (2) zero balance accounts, (3) accounts (including trust accounts) used exclusively for escrow, customs, insurance or fiduciary purposes, (4) merchant accounts, (5) accounts used exclusively for compliance with any Requirements of Law to the extent such Requirements of Law prohibit the granting of a Lien thereon, (6) accounts which constitute cash collateral in respect of a Permitted Lien and (7) any other accounts designated as an Excluded Account by a Responsible Officer of Borrower in writing delivered to the Collateral Agent, the cash balance of which such accounts does not exceed $5,000,000 in the aggregate at any time (all such accounts in sub-clauses (1) through (7) above, collectively, the "**Excluded Accounts**"). Notwithstanding the foregoing, the Credit Parties shall have until the date that is ninety (90) days (or such longer period as the Collateral Agent may agree in its sole discretion) following (i) the Tranche A Closing Date to comply with the provisions of this Section 5.5 with regards to Collateral Accounts of the Credit Parties in existence on the Tranche A Closing Date (or opened during such 90-day period (or such longer period as the Collateral Agent may agree in its sole discretion)) and (ii) the closing date of any Acquisition or other Investment to comply with the provisions of this Section 5.5 with regards to Collateral Accounts of the Credit Parties acquired in connection with such Acquisition or other Investment.

5.6. Compliance with Laws. Comply in all respects with the Requirements of Law and all orders, writs, injunctions, decrees and judgments applicable to it or to its business or its assets or properties (including Environmental Laws, ERISA, Anti-Money Laundering Laws, OFAC, FCPA, Health Care Laws, FDA Laws, DEA Laws, Data Protection Laws and the Federal Fair Labor Standards Act, and any foreign equivalents thereof), except if the failure to comply therewith could not, individually or taken together with any other such failures, reasonably be expected to result in a Material Adverse Change.

5.7. Protection of Intellectual Property Rights.

(a) Except as could not reasonably be expected to result in a Material Adverse Change, (i) protect, defend and maintain the validity and enforceability of the Company IP material to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory, including defending any future or current oppositions, interference proceedings, reissue proceedings, reexamination proceedings, *inter partes* review proceedings, post-grant review proceedings, cancellation proceedings, injunctions, lawsuits, paragraph IV patent certifications or lawsuits under the Hatch-Waxman Act, hearings, investigations, complaints, arbitrations, mediations, demands, International Trade Commission investigations, decrees, or any other disputes, disagreements, or claims, challenging the legality, validity, enforceability or ownership of any Company IP; (ii) maintain the confidential nature of any material trade secrets and trade secret rights used in any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory; and (iii) not allow any Company IP material to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory to be abandoned, forfeited or dedicated to the public or any Current Company IP Agreement to be terminated by Borrower or any of its Subsidiaries, as applicable, without the Collateral Agent's prior written consent (such consent not to be unreasonably withheld, conditioned or delayed); provided, however, that with respect to any such Company IP that is not owned by Borrower or any of its Subsidiaries, the obligations in clauses (i) and (iii) above shall apply only to the extent Borrower or any of its Subsidiaries have the right to take such actions or to cause any licensee or other third party to take such actions pursuant to applicable agreements or contractual rights.

(b) (i) Except as Borrower may otherwise determine in its reasonable business judgment, use commercially reasonable efforts, at its (or its Subsidiaries') sole expense, either directly or indirectly, with respect to any licensee or licensor under the terms of any Credit Party's (or any of its Subsidiary's) agreement with the respective licensee or licensor, as applicable, to take any and all actions (including taking legal action to specifically enforce the applicable terms of any license agreement) and prepare, execute, deliver and file agreements, documents or instruments which are necessary or desirable to (A) prosecute and maintain the Company IP material to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory and (B) diligently defend or assert the Company IP material to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory against material infringement, misappropriation, violation or interference by any other Persons and, in the case of Copyrights, Trademarks and Patents within the Company IP, against any claims of invalidity or unenforceability (including by bringing any legal action for infringement, dilution, violation or defending any counterclaim of invalidity or action of a non-Affiliate third party for declaratory judgment of non-infringement or non-interference); and (ii) use commercially reasonable efforts to cause any licensee or licensor of any Company IP not to, and such Credit Party shall not, disclaim or abandon, or fail to take any action necessary or desirable to prevent the disclaimer or abandonment of Company IP material to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory.

(c) Protect, defend and maintain market exclusivity for the manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory through December 31, 2025, and not allow for the manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of a generic version of any Product in the Territory before December 31, 2025, without the Collateral Agent's prior written consent. Borrower agrees to (i) notify the Collateral Agent in writing of, (ii) keep the Collateral Agent informed regarding, and (iii) at the request of the Collateral Agent in writing, consult with and consider in good faith any comments of the Collateral Agent regarding, any filings in any opposition, interference proceeding, reissue proceeding, reexamination proceeding, *inter partes* review proceeding, post-grant review proceeding, cancellation proceeding, injunction, lawsuit, paragraph IV patent certification or lawsuits under the Hatch-Waxman Act, hearing, investigation, complaint, arbitration, mediation, demand, International Trade Commission investigation, decree, or any other dispute, disagreement, or claim, in each case challenging the legality, validity, enforceability or ownership of any Company IP.

5.8. Books and Records. Maintain proper Books, in which entries that are full, true and correct in all material respects and are in conformity with Applicable Accounting Standards consistently applied shall be made of all material financial transactions and matters involving the assets, properties and business of such Credit Party (or such Subsidiary), as the case may be.

5.9. Access to Collateral; Audits. Allow the Collateral Agent, or its agents or representatives, at any time after the occurrence and during the continuance of an Event of Default, during normal business hours and upon reasonable advance notice, to visit and inspect the Collateral and inspect, copy and audit any Credit Party's Books. The foregoing inspections and audits shall be at the relevant Credit Party's expense.

5.10. Use of Proceeds. (a) Use the proceeds of the Term Loans to fund its general corporate requirements, and (b) not use the proceeds of the Term Loans or any other Credit Extensions, directly or indirectly, for the purpose of purchasing or carrying any Margin Stock, for the purpose of reducing or retiring any Indebtedness that was originally incurred to purchase or carry any Margin Stock, for the purpose of extending credit to any other Person for the purpose of purchasing or carrying any Margin Stock or for any other purpose that might cause any Term Loan or other Credit Extension to be considered a "purpose credit" within the meaning of Regulation T, U or X of the Federal Reserve Board. If requested by the Collateral Agent, Borrower shall complete and sign Part I of a copy of Federal Reserve Form G-3 referred to in Regulation U and deliver such copy to the Collateral Agent.

5.11. Further Assurances. Promptly upon the reasonable written request of the Collateral Agent, execute, acknowledge and deliver such further documents and do such other acts and things in order to effectuate or carry out more effectively the purposes of this Agreement and the other Loan Documents at its expense, including after the Closing Date taking such steps as are reasonably deemed necessary or desirable by the Collateral Agent to maintain, protect and enforce its Lien, for the benefit of Lenders and the other Secured Parties, on Collateral securing the Obligations created under the Security Agreement and the other Loan Documents in accordance with the terms of the Security Agreement and the other Loan Documents, subject to Permitted Liens.

5.12. Additional Collateral; Guarantors.

(a) From and after the Tranche A Closing Date, except as otherwise approved in writing by the Collateral Agent, each Credit Party shall cause each of its Subsidiaries (other than Excluded Subsidiaries) to guarantee the Obligations and to cause each such Subsidiary to grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, a first priority security interest in and Lien upon, and pledge to the Collateral Agent for the benefit of Lenders and the other Secured Parties, subject to Permitted Liens, all of such Subsidiary's properties and assets constituting Collateral, whether now existing or hereafter acquired or existing, to secure such guaranty; provided, that such Credit Party's obligations to cause any Subsidiaries formed or acquired after the Tranche A Closing Date to take the foregoing actions shall be subject to the timing requirements of Section 5.13. Furthermore, except as otherwise approved in writing by the Collateral Agent, each Credit Party, from and after the Tranche A Closing Date, shall, and shall cause each of its Subsidiaries to, grant the Collateral Agent, for the benefit of Lenders and the other Secured Parties, a first priority security interest in and Lien upon, and pledge to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, subject to Permitted Liens, the limitations set forth herein and the limitations set forth in the other Loan Documents, all of the Equity Interests (other than Excluded Equity Interests) in each of its Subsidiaries. Subject to Section 5.14, in connection with each pledge of certificated Equity Interests required under the Loan Documents, the Credit Parties shall deliver, or cause to be delivered, to the Collateral Agent, such certificate(s) together with stock powers or assignments, as applicable, properly endorsed for transfer to the Collateral Agent or duly executed in blank, in each case reasonably satisfactory to the Collateral Agent. Subject to Section 5.14, in connection with each pledge of uncertificated Equity Interests required under the Loan Documents, the Credit Parties shall deliver, or cause to be delivered, to the Collateral Agent an executed uncertificated stock control agreement among the issuer, the registered owner and the Collateral Agent, substantially in the form attached as an Annex to the Security Agreement.

(b) In the event any Credit Party acquires any fee title to real estate in the U.S. with a fair market value (reasonably determined in good faith by a Responsible Officer of Borrower) in excess of $5,000,000, unless otherwise agreed by the Collateral Agent, such Person shall execute or deliver, or cause to be executed or delivered, to the Collateral Agent, (i) within sixty (60) days after such acquisition, an appraisal complying with the Financial Institutions Reform, Recovery and Enforcement Act of 1989, (ii) within forty-five (45) days after receipt of notice from the Collateral Agent that such real estate is located in a Special Flood Hazard Area, Federal Flood Insurance, (iii) within sixty (60) days after such acquisition, a fully executed Mortgage, in form and substance reasonably satisfactory to the Collateral Agent, together with an A.L.T.A. lender's title insurance policy issued by a title insurer reasonably satisfactory to the Collateral Agent, in form and substance (including any endorsements) and in an amount reasonably satisfactory to the Collateral Agent insuring that the Mortgage is a valid and enforceable first priority Lien on the respective property, free and clear of all defects, encumbrances and Liens (other than Permitted Liens), (iv) simultaneously with such acquisition, then-current A.L.T.A. surveys, certified to the Collateral Agent by a licensed surveyor sufficient to allow the issuer of the lender's title insurance policy to issue such policy without a survey exception and (v) within sixty (60) days after such acquisition, an environmental site assessment prepared by a qualified firm reasonably acceptable to the Collateral Agent, in form and substance satisfactory to the Collateral Agent.

5.13. Formation or Acquisition of Subsidiaries. If Borrower or any of its Subsidiaries at any time after the Tranche A Closing Date forms or acquires a Subsidiary (including by division), as promptly as practicable but in no event later than thirty (30) days (or such longer period as the Collateral Agent may agree in its sole discretion) after such formation or acquisition: (a) without limiting the generality of clause (d) below, Borrower will cause such Subsidiary (other than an Excluded Subsidiary) to execute and deliver to the Collateral Agent a joinder to the Security Agreement in the form attached thereto and any relevant IP Agreement or other Collateral Documents, as applicable; (b) Borrower will deliver to the Collateral Agent (i) true, correct and complete copies of the Operating Documents of such Subsidiary (other than an Excluded Subsidiary), (ii) a Secretary's Certificate, certifying that the copies of the Operating Documents of such Subsidiary (other than an Excluded Subsidiary) are true, correct and complete (such Secretary's Certificate to be in form and substance reasonably satisfactory to the Collateral Agent) and (iii) a good standing certificate for such Subsidiary (other than an Excluded Subsidiary) certified by the Secretary of State (or the equivalent thereof) of its jurisdiction of organization, incorporation or formation; (c) Borrower will deliver to the

Collateral Agent a Perfection Certificate, updated to reflect the formation or acquisition of such Subsidiary; and (d) Borrower will cause such Subsidiary to satisfy all requirements contained in this Agreement (including Section 5.12) and each other Loan Document if and to the extent applicable to such Subsidiary. Borrower, Lenders and the Collateral Agent hereby agree that any such Subsidiary (other than an Excluded Subsidiary) shall constitute a Credit Party for all purposes hereunder as of the date of the execution and delivery of the joinder contemplated by clause (a) above. Any document, agreement or instrument executed or issued pursuant to this Section 5.13 shall be a Loan Document.

5.14. Post-Closing Requirements. Borrower will, and will cause each of its Subsidiaries to, take each of the actions set forth on Schedule 5.14 of the Disclosure Letter within the time period prescribed therefor on such schedule (or such longer period as the Collateral Agent may agree in its sole discretion), which shall include, among other things, that notwithstanding anything to the contrary in Section 5.5, the Credit Parties shall have until the date that is ninety (90) days following the Tranche A Closing Date (or such longer period as the Collateral Agent may agree in its sole discretion) to comply with the provisions of Section 5.5 with regards to Collateral Accounts of the Credit Parties in existence on the Tranche A Closing Date or opened during such 90-day period (or such longer period as the Collateral Agent may agree in its sole discretion). All representations and warranties and covenants contained in this Agreement and the other Loan Documents shall be deemed modified to the extent necessary to take the actions set forth on Schedule 5.14 of the Disclosure Letter within the time periods set forth therein, rather than elsewhere provided in the Loan Documents, such that to the extent any such action set forth in Schedule 5.14 of the Disclosure Letter is not overdue, the applicable Credit Party shall not be in breach of any representation or warranty or covenant contained in this Agreement or any other Loan Document applicable to such action for the period from the Tranche A Closing Date until the date on which such action is required to be fulfilled as set forth on Schedule 5.14 of the Disclosure Letter.

5.15. Environmental.

(a) Deliver to the Collateral Agent:

(i) as soon as practicable following receipt thereof, copies of all environmental audits, investigations, analyses and reports of any kind or character, whether prepared by personnel of Borrower or any of its Subsidiaries or by independent consultants, governmental authorities or any other Persons, with respect to significant environmental matters at any Facility or with respect to any material Environmental Claims;

(ii) promptly upon a Responsible Officer of any Credit Party or any of its Subsidiaries obtaining knowledge of the occurrence thereof, written notice describing in reasonable detail (A) any Release required to be reported to any federal, state or local governmental or regulatory agency under any applicable Environmental Laws, (B) any remedial action taken by any Credit Party or any other Person in response to (x) any Hazardous Materials Activities, the existence of which, individually or in the aggregate, could reasonably be expected to result in one or more Environmental Claims resulting in a Material Adverse Change, or (y) any Environmental Claims that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change, and (C) any Credit Party's discovery of any occurrence or condition on any real property adjoining or in the vicinity of any Facility that could cause such Facility or any part thereof to be subject to any material restrictions on the ownership, occupancy, transferability or use thereof under any Environmental Laws, provided, that with respect to real property adjoining or in the vicinity of any Facility, Borrower shall have no duty to affirmatively investigate or make any efforts to become or stay informed regarding any such adjoining or nearby properties;

(iii) as soon as practicable following the sending or receipt thereof by any Credit Party, a copy of any and all written communications with respect to (A) any Environmental Claims that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change, (B) any Release required to be reported to any federal, state or local governmental or regulatory agency, or (C) any request for information from any Governmental Authority that suggests such Governmental Authority is investigating whether any Credit Party or any of its Subsidiaries may be potentially responsible for any Hazardous Materials Activity that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change;

(iv) prompt written notice describing in reasonable detail (A) any proposed acquisition of stock, assets, or property by Borrower or any of its Subsidiaries that, individually or in the aggregate, could reasonably be expected to (x) expose Borrower or any of its Subsidiaries to, or result in, Environmental Claims that could reasonably be expected to result in a Material Adverse Change or (y) affect the ability of Borrower or any of its Subsidiaries to maintain in full force and effect all material Governmental Approvals required under any Environmental Laws for their respective operations, and (B) any proposed action to be taken by Borrower or any of its Subsidiaries to modify current operations in a manner that, individually or taken together with any other such proposed actions, could reasonably be expected to subject Borrower or any of its Subsidiaries to any additional material obligations or requirements under any Environmental Laws; and

(v) with reasonable promptness, such other documents and information as from time to time may be reasonably requested by the Collateral Agent in relation to any matters disclosed pursuant to this Section 5.15(a).

(b) Each Credit Party shall, and shall cause each of its Subsidiaries to, promptly take any and all actions reasonably necessary to (i) cure any violation of applicable Environmental Laws by Borrower or any of its Subsidiaries that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change, and (ii) make an appropriate response to any Environmental Claim against Borrower or any of its Subsidiaries and discharge any obligations it may have to any Person thereunder where failure to do so, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Change.

5.16. Inventory; Returns; Maintenance of Properties. Keep all Inventory in good and marketable condition, free from material defects and otherwise keep all Inventory in material compliance with all applicable FDA Good Manufacturing Practices, Good Clinical Practice, and Good Laboratory Practices, as applicable. Returns and allowances between Borrower and its Account Debtors shall follow Borrower's customary practices as they exist at the Effective Date or, solely with respect to the Acquired Business, any new returns and allowances practices established thereafter in good faith by Borrower. Each Credit Party will, and will cause each of its Subsidiaries to, maintain or cause to be maintained in good repair, working order and condition, ordinary wear and tear, casualty and condemnation excepted, all material tangible properties used or useful in its respective business, and from time to time will make or cause to be made all appropriate repairs, renewals and replacements thereof except where failure to do so could not reasonably be expected to result in a Material Adverse Change.

5.17. Regulatory Obligations, Maintenance of FDA Approval, Manufacturing, Marketing, and Distribution. (i) Comply with FDA post-marketing approval requirements for the Product in the Territory, (ii) maintain the FDA approval to manufacture, market, and distribute the Product in the Territory, and (iii) continue the manufacturing, marketing, and distribution of the Product in the Territory. Report to Collateral Agent any instances where the Credit Party or any of its Subsidiaries has a reasonable expectation that there are grounds for imposition of a clinical hold, as described in 21 C.F.R. § 312.42.

6 NEGATIVE COVENANTS

Each Credit Party covenants and agrees that, until payment in full of all Obligations (other than inchoate indemnity obligations), such Credit Party shall not, and shall cause each of its Subsidiaries not to:

6.1. Dispositions. Convey, sell, lease, transfer, assign, covenant not to sue, enter into a coexistence agreement, exclusively or non-exclusively license out, or otherwise dispose of (including any sale-leaseback or any transfer of assets pursuant to a plan of division), directly or indirectly and whether in one or a series of transactions (collectively, "**Transfer**"), all or any part of its properties or assets constituting Collateral or any Company IP that does not constitute Collateral under the Loan Documents but is related to any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of the Product in the Territory; except, in each case of this Section 6.1, for Permitted Transfers (unless otherwise expressly prohibited under in Section 6.6(b)).

6.2. Fundamental Changes; Location of Collateral.

(a) Without at least ten (10) days prior written notice to the Collateral Agent, solely in the case of a Credit Party: (i) change its jurisdiction of organization, incorporation or formation, (ii) change its organizational structure or type, (iii) change its legal name, or (iv) change any organizational number (if any) assigned by its jurisdiction of organization, incorporation or formation.

(b) Not deliver any material portion of the Collateral to one or more leased locations or bailees, unless (i) such Credit Party has delivered at least fifteen (15) days' prior written notice to the Collateral Agent, which such notice shall in reasonable detail identify such Collateral and indicate the location from which it is being delivered and the location to which it is being delivered (and may be in the form of an updated Perfection Certificate; provided that any update to the Perfection Certificate by any Credit Party pursuant to this Section 6.2(b) shall not relieve any Credit Party of any other Obligation under this Agreement, including under clause (ii) below), and (ii) the Collateral Agent and such landlord or bailee are already parties to a landlord's consent in favor of the Collateral Agent, for the benefit of the Lenders and the other Secured Parties, for such leased location or a bailee agreement governing both such Collateral and the location to which such Collateral will be delivered (in form and substance reasonably satisfactory to the Collateral Agent).

6.3. Mergers, Acquisitions, Liquidations or Dissolutions.

(a) Merge, divide itself into two (2) or more entities, consolidate, liquidate or dissolve, or permit any of its Subsidiaries to merge, divide itself into two (2) or more entities, consolidate, liquidate or dissolve with or into any other Person, except that:

(i) any Subsidiary of Borrower may merge or consolidate with or into Borrower, provided that Borrower is the surviving entity,

(ii) any Subsidiary of Borrower may merge or consolidate with any other Subsidiary of Borrower, provided that if any party to such merger or consolidation is a Credit Party then either (x) such Credit Party is the surviving entity or (y) the surviving or resulting entity executes and delivers to the Collateral Agent a joinder to the Security Agreement in the form attached thereto and any relevant IP Agreement or other Collateral Documents, as applicable, and otherwise satisfies the requirements of Section 5.13 substantially contemporaneously with completion of such merger or consolidation to;

(iii) any Subsidiary of Borrower may divide itself into two (2) or more entities or be dissolved or liquidated, provided that the properties and assets of such Subsidiary are allocated or distributed to an existing or newly-formed Credit Party; and

(iv) any Permitted Investment may be structured as a merger or consolidation; or

(b) make, or permit any of its Subsidiaries to make, Acquisitions outside the ordinary course of business, including any purchase of the assets of any division or line of business of any other Person, other than Permitted Acquisitions or Permitted Investments.

6.4. Indebtedness. Directly or indirectly, create, incur, assume or guaranty, or otherwise become or remain directly or indirectly liable with respect to, any Indebtedness (including any Indebtedness consisting of obligations evidenced by a bond, debenture, note or other similar instrument) that is not Permitted Indebtedness; provided, however, that the accrual of interest, the accretion of accreted value and the payment of interest in the form of additional Indebtedness shall not be deemed to be an incurrence of Indebtedness for purposes of this Section 6.4.

6.5. Encumbrances. Except for Permitted Liens, (i) create, incur, allow, or suffer to exist any Lien on any Collateral, or (ii) permit (other than pursuant to the terms of the Loan Documents) any material portion of the Collateral not to be subject to the first priority security interest granted in the Loan Documents or otherwise pursuant to the Collateral Documents, in each case of this clause (ii), other than as a direct result of any action by the Collateral Agent or any Lender or failure of the Collateral Agent or any Lender to perform an obligation thereof under the Loan Documents.

6.6. No Further Negative Pledges; Negative Pledge.

(a) No Credit Party nor any of its Subsidiaries shall enter into any agreement, document or instrument directly or indirectly prohibiting (or having the effect of prohibiting) or limiting the ability of such Credit Party or Subsidiary to create, incur, assume or suffer to exist any Lien upon any Collateral, whether now owned or hereafter acquired, in favor of the Collateral Agent, for the benefit of Lenders and the other Secured Parties, with respect to the Obligations or under the Loan Documents, in each case of this Section 6.6, other than Permitted Negative Pledges.

(b) Notwithstanding Section 6.1, no Credit Party will sell, assign, transfer, exchange or otherwise dispose of, or create, incur, allow or suffer to exist any Lien on, any Equity Interests constituting Collateral issued by any Subsidiary which are owned or otherwise held by such Credit Party, except for: (i) Permitted Liens; (ii) transfers between or among Credit Parties, provided that any and all steps as may be required to be taken in order to create and maintain a first priority security interest in and Lien upon such Equity Interests in favor of the Collateral Agent, for the benefit of Lenders and the other Secured Parties, are taken contemporaneously with the completion of any such transfer; and (iii) sales, assignments, transfers, exchanges or other dispositions to qualify directors if required by Requirements of Law or otherwise permitted under this Agreement, provided that such sale, assignment, transfer, exchange or other disposition shall be for the minimum number of Equity Interests as are necessary for such qualification under Requirements of Law.

6.7. Maintenance of Collateral Accounts. Maintain any Collateral Account except pursuant to the terms of Section 5.5 hereof.

6.8. Distributions; Investments.

(a) Pay any dividends or make any distribution or payment on or redeem, retire or purchase any Equity Interests, except, in each case of this Section 6.8, for Permitted Distributions.

(b) Directly or indirectly make any Investment other than Permitted Investments.

6.9. No Restrictions on Subsidiary Distributions. No Credit Party nor any of its Subsidiaries shall enter into any agreement, document or instrument directly or indirectly prohibiting (or having the effect of prohibiting) or limiting the ability of any Subsidiary of Borrower to (a) pay dividends or make any other distributions on any of such Subsidiary's Equity Interests owned by Borrower or any other Subsidiary of Borrower, (b) repay or prepay any Indebtedness owed by such Subsidiary to Borrower or any other Subsidiary of Borrower, (c) make loans or advances to Borrower or any other Subsidiary of Borrower, or (d) transfer, lease or license any Collateral to Borrower or any other Subsidiary of Borrower, except, in each case of this Section 6.9, for Permitted Subsidiary Distribution Restrictions.

6.10. Subordinated Debt. Make or permit any voluntary or optional prepayment of any Subordinated Debt.

6.11. Amendments or Waivers of Organizational Documents. Amend, restate, supplement or otherwise modify, or waive, any provision of its Operating Documents in a manner that would reasonably be expected to result in a Material Adverse Change.

6.12. Compliance.

(a) Become an "investment company" under the Investment Company Act of 1940, or undertake as one of its important activities extending credit to purchase or carry margin stock (as defined in Regulation U of the Board of Governors of the Federal Reserve System), or use the proceeds of any Credit Extension for that purpose;

(b) No ERISA Affiliate shall cause or suffer to exist (i) any event that would result in the imposition of a Lien on any assets or properties of any Credit Party or a Subsidiary of a Credit Party with respect to any Plan or Multiemployer Plan or (ii) any other ERISA Event that, in the case of clauses (i) and (ii), could reasonably be expected to, individually or in the aggregate, result in a Material Adverse Change; or

(c) Permit the occurrence of any other event with respect to any present pension, profit sharing or deferred compensation plan which could reasonably be expected to result in a Material Adverse Change.

6.13. Compliance with Sanctions and Anti-Money Laundering Laws. The Collateral Agent and each Lender hereby notifies each Credit Party that pursuant to the requirements of Sanctions and Anti-Money Laundering Laws, and such Person's policies and practices, the Collateral Agent and each Lender is required to obtain, verify and record certain information and documentation that identifies each Credit Party and its principals, which information includes the name and address of each Credit Party and its principals and such other information that will allow the Collateral Agent and each Lender to identify such party in accordance with Sanctions and Anti-Money Laundering Laws. No Credit Party will, nor will any Credit Party permit any of its Subsidiaries or controlled Affiliates to, directly or indirectly, knowingly enter into any documents or contracts with any Blocked Person. Each Credit Party shall promptly (but in any event within three (3) Business Days) notify the Collateral Agent and each Lender in writing upon any Responsible Officer of Borrower having knowledge that any Credit Party or any Subsidiary or Affiliate of any Credit Party is a Blocked Person or (a) is convicted on, (b) pleads nolo contendere to, (c) is indicted on, or (d) is arraigned and held over on charges involving money laundering or predicate crimes to money laundering. No Credit Party will, nor will any Credit Party permit any of its Subsidiaries or Affiliates to, directly or indirectly, (i) conduct any business or engage in any transaction or dealing with any Blocked Person, including the making or receiving of any contribution of funds, goods or services to or for the benefit of any Blocked Person, (ii) deal in, or otherwise engage in any transaction relating to, any property or interests in property blocked pursuant to Sanctions, or (iii) engage in or conspire to engage in any transaction that evades or avoids or violates, or has the purpose of evading or avoiding, or attempts to violate, any of prohibitions under applicable Sanctions or Anti-Money Laundering Laws.

6.14. Amendments or Waivers of Current Company IP Agreements. (a) Waive, amend, cancel or terminate, exercise or fail to exercise, any material rights constituting or relating to any of the Current Company IP Agreements or (b) breach, default under, or take any action or fail to take any action that, with the passage of time or the giving of notice or both, would constitute a default or event of default under any of the Current Company IP Agreements, in each case of this Section 6.14, which could reasonably be expected to, individually or taken together with any other such waivers, amendments, cancellations, terminations, exercises or failures, result in a Material Adverse Change.

7 EVENTS OF DEFAULT

Any one of the following shall constitute an event of default (an "**Event of Default**") under this Agreement:

7.1. Payment Default. Any Credit Party fails to (a) make any payment of any principal of the Term Loan when and as the same shall become due and payable, whether at the due date thereof (including pursuant to Section 2.2(c)) or at a date fixed for prepayment (whether voluntary or mandatory) thereof or by acceleration thereof or otherwise, or (b) within five (5) Business Days after the same becomes due, any payment of interest or premium pursuant to Section 2.2, including any applicable Additional Consideration, Makewhole Amount or Prepayment Premium, or any other Obligations (which five (5) Business Day cure period shall not apply to any such payments due on the Term Loan Maturity Date, such earlier date pursuant to Section 2.2(c)(ii) hereof or the date of acceleration pursuant to Section 8.1(a) hereof). A failure to pay any such interest, premium or Obligations pursuant to the foregoing clause (b) prior to the end of such five (5) Business Day-period shall not constitute an Event of Default (unless such payment is due on the Term Loan Maturity Date, such earlier date pursuant to Section 2.2(c)(ii) hereof or the date of acceleration pursuant to Section 8.1(a) hereof).

7.2. Covenant Default.

(a) The Credit Parties: (i) fail or neglect to perform any obligation in Sections 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.10, 5.12, 5.13, 5.14 5.16 or 5.17 or (ii) violate any covenant in Section 6; or

(b) The Credit Parties fail or neglect to perform, keep, or observe any other term, provision, condition, covenant or agreement contained in this Agreement or any Loan Documents on its part to be performed, kept or observed and such failure continues for ten (10) days, after the earlier of the date on which (i) a Responsible Officer of any Credit Party becomes aware of such failure and (ii) written notice thereof shall have been given to the Borrower by the Collateral Agent or any Lender. Cure periods provided under this Section 7.2(b) shall not apply, among other things, to any of the covenants referenced in clause (a) above.

7.3. Material Adverse Change. A Material Adverse Change of the type described in clause (iii) or clause (iv) of the definition of "Material Adverse Change" occurs.

7.4. Attachment; Levy; Restraint on Business.

(a) (i) The service of process seeking to attach, by trustee or similar process, any funds of any Credit Party or of any entity under the control of any Credit Party (including a Subsidiary) in excess of $10,000,000 on deposit or otherwise maintained with the Collateral Agent, or (ii) a notice of lien or levy is filed against any of material portion of Collateral by any Governmental Authority, and the same under sub-clauses (i) and (ii) hereof are not, within thirty (30) days after the occurrence thereof, discharged or stayed (whether through the posting of a bond or otherwise); provided, however, that no Credit Extensions shall be made during any thirty (30) day cure period; or

(b) (i) Any material portion of Collateral is attached, seized, levied on, or comes into possession of a trustee or receiver, or (ii) any court order enjoins, restrains, or prevents Borrower and its Subsidiaries from conducting any material part of their business, taken as a whole.

7.5. Insolvency.

(a) An involuntary proceeding shall be commenced or an involuntary petition shall be filed in a court of competent jurisdiction seeking: (i) relief in respect of any Credit Party, or of a substantial part of the property of any Credit Party, under Title 11 of the United States Code, as now constituted or hereafter amended, or any other federal, state or foreign bankruptcy, insolvency, receivership or similar law; (ii) the appointment of a receiver, trustee, custodian, sequestrator, conservator or similar official for any Credit Party or for a substantial part of the property or assets of any Credit Party; or (iii) the winding-up or liquidation of any Credit Party, and such proceeding or petition shall continue undismissed or unstayed for sixty (60) days or an order or decree approving or ordering any of the foregoing shall be entered; or

(b) Any Credit Party shall: (i) voluntarily commence any proceeding or file any petition seeking relief under Title 11 of the United States Code, as now constituted or hereafter amended, or any other federal, state or foreign bankruptcy, insolvency, receivership or similar law; (ii) consent to the institution of, or fail to contest in a timely and appropriate manner, any proceeding or the filing of any petition described in clause (a) above; (iii) apply for or consent to the appointment of a receiver, trustee, custodian, sequestrator, conservator or similar official for any Credit Party or for a substantial part of the property or assets of any Credit Party; (iv) file an answer admitting the material allegations of a petition filed against it in any such proceeding; (v) make a general assignment for the benefit of creditors; (vi) become unable, admit in writing its inability or fail generally to pay its debts as they become due; (vii) take any action for the purpose of effecting any of the foregoing; or (viii) wind up or liquidate (except as otherwise expressly permitted hereunder).

7.6. Other Agreements. Any Credit Party fails to pay any Indebtedness (other than the Indebtedness represented by this Agreement and the other Loan Documents) within any applicable grace period after such payment is due and payable (including at final maturity) or after the acceleration of any such Indebtedness by the holder(s) thereof because of a default, in each case, if the total amount of such Indebtedness unpaid or accelerated exceeds $10,000,000.

7.7. Judgments. One or more final, non-appealable judgments, orders, or decrees for the payment of money in an amount in excess of $10,000,000 (but excluding any final judgments, orders, or decrees for the payment of money that are covered by independent third-party insurance as to which liability has not been denied by such insurance carrier or by an indemnification claim against a solvent and unaffiliated Person that is not a Credit Party as to which such Person has not denied liability for such claim), shall be rendered against one or more Credit Parties and the same are not, within thirty (30) days after the entry thereof, discharged or execution thereof stayed or bonded pending appeal, or such judgments are not discharged prior to the expiration of any such stay.

7.8. Misrepresentations. Any Credit Party or any Person acting for any Credit Party makes or is deemed to make any representation, warranty, or other statement now or later in this Agreement, any other Loan Document or in any writing delivered to the Collateral Agent or any Lender or to induce the Collateral Agent or any Lender to enter this Agreement or any other Loan Document, and such representation, warranty, or other statement is incorrect in any material respect (or, to the extent any such representation, warranty or other statement is qualified by materiality or Material Adverse Change, in any respect) when made or deemed to be made.

7.9. Loan Documents; Collateral. Any material provision of any Loan Document shall for any reason cease to be valid and binding on or enforceable against any Credit Party, or any Credit Party shall so state in writing or bring an action to limit its obligations or liabilities thereunder; or any Collateral Document shall for any reason (other than pursuant to the terms thereof) cease to create a valid security interest in any material portion of the Collateral purported to be covered thereby or such security interest shall for any reason (other than pursuant to the terms of the Loan Documents) cease to be a perfected and first priority security interest in any material portion of the Collateral subject thereto, subject only to Permitted Liens, in each case, other than as a direct result of any action by the Collateral Agent or any Lender or failure of the Collateral Agent or any Lender to perform an obligation thereof under the Loan Documents.

7.10. ERISA Event. An ERISA Event occurs that, individually or taken together with any other ERISA Events, results or could reasonably be expected to result in a Material Adverse Change or the imposition of a Lien on any Collateral.

8 RIGHTS AND REMEDIES UPON AN EVENT OF DEFAULT

8.1. Rights and Remedies. While an Event of Default occurs and continues, the Collateral Agent may, or at the request of the Required Lenders, will, without notice or demand:

(a) declare all Obligations (including, for the avoidance of doubt, the Makewhole Amount or Prepayment Premium that is payable pursuant to Section 2.2(e) and Section 2.2(f), as applicable) immediately due and payable (but if an Event of Default described in Section 7.5 occurs all Obligations, including the Makewhole Amount and Prepayment Premium that is payable pursuant to Section 2.2(e) and Section 2.2(f), as applicable, are automatically and immediately due and payable without any action by the Collateral Agent or any Lender), whereupon all Obligations for principal, interest, premium or otherwise (including, for the avoidance of doubt, the Makewhole Amount and Prepayment Premium that is payable pursuant to Section 2.2(e) and Section 2.2(f), as applicable) shall become due and payable by Borrower without presentment, demand, protest or other notice of any kind, which are all expressly waived by the Credit Parties hereby;

(b) stop advancing money or extending credit for Borrower's benefit under this Agreement;

(c) settle or adjust disputes and claims directly with Account Debtors for amounts on terms and in any order that the Collateral Agent considers advisable, notify any Person owing Borrower money of the Collateral Agent's security interest, for the benefit of the Lenders and the other Secured Parties, in such funds, and verify the amount of the Collateral Accounts;

(d) make any payments and do any acts it considers necessary or reasonable to protect the Collateral or the Collateral Agent's security interest, for the benefit of Lenders and the other Secured Parties, in the Collateral. Borrower shall assemble the Collateral if the Collateral Agent or the Required Lenders requests and make it available as the Collateral Agent designates or the Required Lenders designate. The Collateral Agent or its agents or representatives may enter premises where the Collateral is located, take and maintain possession of any part of the Collateral, and pay, purchase, contest, or compromise any Lien that appears to be prior or superior to its security interest, for the benefit of Lenders and the other Secured Parties, and pay all expenses incurred. Borrower grants the Collateral Agent a license to enter and occupy (and for its agents or representatives to enter and occupy) any of its premises, without charge, to exercise any of the Collateral Agent's or any Lender's rights or remedies;

(e) apply to the Obligations (i) any balances and deposits of Borrower it holds, or (ii) any amount held by the Collateral Agent owing to or for the credit or the account of Borrower;

(f) ship, reclaim, recover, store, finish, maintain, repair, prepare for sale, advertise for sale, and sell the Collateral. With respect to any and all Intellectual Property owned by any Credit Party and included in Collateral, each Credit Party hereby grants to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, as of the Tranche A Closing Date, a non-exclusive, royalty-free license or other right to use, without charge, such Intellectual Property in advertising for sale and selling any Collateral and, in connection with the Collateral Agent's exercise of its rights under this Section 8.1, Borrower's rights under all licenses and all franchise Contracts inure to the benefit of all Secured Parties. Each Credit Party shall retain the right to control the Collateral Agent's use of its trade names and Trademarks and such trade names and Trademarks, together with the goodwill associated therewith, are and remain the exclusive property of the Credit Parties, and any and all use of the same by the Collateral Agent shall inure to the benefit of the Credit Parties;

(g) place a "hold" on any account maintained with the Collateral Agent or deliver a notice of exclusive control, any entitlement order, or other directions or instructions pursuant to any Control Agreement or similar agreements providing control of any Collateral;

(h) demand and receive possession of Borrower's Books regarding Collateral; and

(i) exercise all rights and remedies available to the Collateral Agent or any Lender under the Collateral Documents or any other Loan Documents or at law or equity, including all remedies provided under the Code (including disposal of the Collateral pursuant to the terms thereof).

Each of the Collateral Agent and Lender agrees that in connection with any foreclosure or other exercise of rights under this Agreement or any other Loan Document with respect to any Intellectual Property included in the Collateral, the rights of the licensees under any license of such Intellectual Property will not be terminated, limited or otherwise adversely affected so long as no default exists thereunder in a way that would permit the licensor to terminate such license (commonly termed a non-disturbance). Without limitation to any other provision herein or in any other Loan Document, while an Event of Default occurs and continues, at the Collateral Agent's or the Required Lenders' request, representatives from Borrower and the Collateral Agent shall promptly meet (in person or telephonically) to discuss in good faith how to collect, receive, appropriate and realize upon Borrower's rights and interests in, to and under any Current Company IP Agreement, including in connection with any foreclosure or other exercise of the Collateral Agent's or any Lender's rights with respect thereto. If Borrower and the Collateral Agent do not mutually agree with respect thereto within ten (10) Business Days after such request by the Collateral Agent (or such later date as agreed by the Collateral Agent), then the Collateral Agent may request Borrower to, and Borrower (promptly following the receipt of such request) shall, use reasonable best efforts to obtain the written consent of any counterparty to the exercise by the Collateral Agent or any Lender of any and all rights and remedies under this Agreement or any other Loan Document with respect to any Current Company IP Agreement, in form and substance reasonably satisfactory to the Collateral Agent.

8.2. Power of Attorney. Borrower hereby irrevocably appoints the Collateral Agent and any Related Party thereof as its lawful attorney-in-fact, exercisable upon the occurrence and during the continuance of an Event of Default, to: (a) endorse Borrower's name on any checks or other forms of payment or security; (b) sign Borrower's name on any invoice or bill of lading for any Account or drafts against Account Debtors; (c) settle and adjust disputes and claims about the Collateral Accounts directly with depository banks where the Collateral Accounts are maintained, for amounts and on terms the Collateral Agent determines reasonable; (d) make, settle, and adjust all claims under Borrower's products liability or general liability insurance policies maintained in the United States regarding Collateral; (e) pay, contest or settle any Lien, charge, encumbrance, security interest, and adverse claim in or to the Collateral, or any judgment based thereon, or otherwise take any action to terminate or discharge the same; and (f) transfer the Collateral into the name of the Collateral Agent or a third party as the Code permits. Borrower hereby appoints the Collateral Agent and any Related Party thereof as its lawful attorney-in-fact to file or record any documents necessary to perfect or continue the perfection of the Collateral Agent's security interest, for the benefit of

Lenders and the other Secured Parties, in the Collateral regardless of whether an Event of Default has occurred until all Obligations (other than inchoate indemnity obligations) have been satisfied in full and no Lender is under any further obligation to make Credit Extensions hereunder. The foregoing appointment of the Collateral Agent and any Related Party thereof as Borrower's attorney in fact, and all of the Collateral Agent's (or such Related Party's) rights and powers, coupled with an interest, are irrevocable until all Obligations (other than inchoate indemnity obligations) have been fully repaid and performed and each Lender's obligation to provide Credit Extensions terminates.

8.3. Application of Payments and Proceeds Upon Default. If an Event of Default has occurred and is continuing, the Collateral Agent shall apply any funds in its possession, whether from Borrower account balances, payments, proceeds realized as the result of any collection of Collateral Accounts or disposition of any other Collateral, or otherwise, to the Obligations in such order as the Collateral Agent shall determine in its sole discretion. Any surplus shall be paid to Borrower or other Persons legally entitled thereto; Borrower shall remain liable to Lenders for any deficiency. If the Collateral Agent or any Lender directly or indirectly enters into a deferred payment or other credit transaction with any purchaser at any sale of Collateral, the Collateral Agent or such Lender, as applicable, shall have the option, exercisable at any time, of either reducing the Obligations by the principal amount of the purchase price or deferring the reduction of the Obligations until the actual receipt by the applicable Lender(s) of cash therefor.

8.4. Collateral Agent's Liability for Collateral. So long as the Collateral Agent complies with Requirements of Law regarding the safekeeping of the Collateral in the possession or under the control of the Collateral Agent, the Collateral Agent shall not be liable or responsible for: (a) the safekeeping of the Collateral; (b) any loss or damage to the Collateral; or (c) any act or default of any other Person. In no event shall the Collateral Agent or any Lender have any liability for any diminution in the value of the Collateral for any reason. Borrower bears all risk of loss, damage or destruction of the Collateral.

8.5. No Waiver; Remedies Cumulative. The Collateral Agent's or any Lender's failure, at any time or times, to require strict performance by Borrower of any provision of this Agreement or any other Loan Document shall not waive, affect, or diminish any right of the Collateral Agent or any Lender thereafter to demand strict performance and compliance herewith or therewith. No waiver hereunder shall be effective unless signed by the party granting the waiver and then is only effective for the specific instance and purpose for which it is given. Each of the Collateral Agent's and Lender's rights and remedies under this Agreement and the other Loan Documents are cumulative. Each of the Collateral Agent and Lenders has all rights and remedies provided under the Code, by law, or in equity. The exercise by the Collateral Agent or any Lender of one right or remedy is not an election and shall not preclude the Collateral Agent or any Lender from exercising any other remedy under this Agreement or other remedy available at law or in equity, and the waiver by the Collateral Agent or any Lender of any Event of Default is not a continuing waiver. The Collateral Agent's or any Lender's delay in exercising any remedy is not a waiver, election, or acquiescence.

8.6. Demand Waiver; Makewhole Amount; Prepayment Premium. Borrower waives demand, notice of default or dishonor, notice of payment and nonpayment, notice of any default, nonpayment at maturity, release, compromise, settlement, extension, or renewal of accounts, documents, instruments, chattel paper, and guarantees held by the Collateral Agent on which Borrower is liable. Borrower acknowledges and agrees that if the maturity of all Obligations shall be accelerated pursuant to Section 8.1(a) by reason of the occurrence of an Event of Default, the applicable Makewhole Amount and Prepayment Premium that is payable pursuant to Section 2.2(e) and Section 2.2(f) shall become due and payable by Borrower upon such acceleration, whether such acceleration is automatic or is effected by the Collateral Agent's or any Lender's declaration thereof, as provided in Section 8.1(a), and Borrower shall pay the applicable Makewhole Amount and Prepayment Premium that is payable pursuant to Section 2.2(e) and Section 2.2(f) as compensation to Lenders for the loss of its investment opportunity and not as a penalty, and Borrower waives any right to object thereto in any voluntary or involuntary bankruptcy, insolvency or similar proceeding or otherwise.

9 NOTICES

All notices, consents, requests, approvals, demands, or other communication by any party to this Agreement or any other Loan Document must be in writing and shall be deemed to have been validly served, given, or delivered: (a) upon the earlier of actual receipt and three (3) Business Days after deposit in the U.S. mail, first class, registered or certified mail return receipt requested, with proper postage prepaid; (b) upon transmission, when sent by electronic

mail or facsimile transmission; (c) one (1) Business Day after deposit with a reputable overnight courier with all charges prepaid; or (d) when delivered, if hand-delivered by messenger, all of which shall be addressed to the party to be notified and sent to the address, facsimile number, or email address (if any) indicated below. Any party to this Agreement may change its mailing or electronic mail address or facsimile number by giving all other parties hereto written notice thereof in accordance with the terms of this Section 9.

If to Borrower or any other Credit Party:

Global Blood Therapeutics, Inc.
171 Oyster Point Boulevard, Suite 300
South San Francisco, CA 94080
Attn: Chief Legal Officer
Telephone: (650) 351.4756
Facsimile: (650) 351.4756

with a copy to (which shall not constitute notice) to:

Goodwin Procter LLP
Three Embarcadero Center
28th Floor
San Francisco, California 94111
Attn: William Burnet Pearce
Telephone: (415) 733-6031
Facsimile: (415) 384-6015
Email: WPearce@goodwinlaw.com

If to Collateral Agent: BioPharma Credit PLC
c/o Beaufort House
51 New North Road
Exeter EX4 4EP
United Kingdom
Attn: Company Secretary
Tel: +44 01 392 477 500
Fax: +44 01 392 253 282
Email: Pharmakon@Pharmakonadvisors.com

with copies (which shall not constitute notice) to:

Pharmakon Advisors LP
110 East 59th Street, #3300
New York, NY 10022
Attn: Pedro Gonzalez de Cosio
Phone: +1 (212) 883-2296
Fax: +1 (917) 210-4048
Email: Pharmakon@Pharmakonadvisors.com

and

Akin Gump Strauss Hauer & Feld LLP
One Bryant Park
New York, NY 10036-6745
Attn: Geoffrey E. Secol; Jonathan Pavlich
Phone: (212) 872-8081; (212) 872-8013
Fax: (212) 872-1002
Email: gsecol@akingump.com; jpavlich@akingump.com

If to any Lender: To the address set forth on Exhibit D attached hereto.

10 CHOICE OF LAW, VENUE, AND JURY TRIAL WAIVER

THE LOAN DOCUMENTS SHALL BE GOVERNED BY, AND CONSTRUED AND INTERPRETED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK, WITHOUT REGARD TO ANY PRINCIPLES OF CONFLICTS OF LAW THAT COULD REQUIRE THE APPLICATION OF THE LAW OF ANY OTHER JURISDICTION. Each party hereto submits to the exclusive jurisdiction of the courts of the State of New York sitting in New York County, and of the United States District Court of the Southern District of New York, and any appellate court from any thereof, and agrees that all claims in respect of any such action, litigation or proceeding may be heard and determined in such New York State court or, to the fullest extent permitted by Requirements of Law, in such Federal court; provided, however, that nothing in this Agreement shall be deemed to operate to preclude the Collateral Agent or any Lender from bringing suit or taking other legal action in any other jurisdiction to realize on the Collateral or any other security for the Obligations, or to enforce a judgment or other court order in favor of the Collateral Agent or any Lender. Each Credit Party expressly submits and consents in advance to such jurisdiction in any action or suit commenced in any such court, and each Credit Party hereby waives any objection that it may have based upon lack of personal jurisdiction, improper venue, or *forum non conveniens* and hereby consents to the granting of such legal or equitable relief as is deemed appropriate by such court. Each Credit Party hereby waives personal service of the summons, complaints, and other process issued in such action or suit and agrees that service of such summons, complaints, and other process may be made by registered or certified mail addressed to such party at the address set forth in (or otherwise provided in accordance with the terms of) Section 9 of this Agreement and that service so made shall be deemed completed upon the earlier to occur of such party's actual receipt thereof or three (3) days after deposit in the U.S. mails, proper postage prepaid.

TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, EACH PARTY HERETO WAIVES ITS RIGHT TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION ARISING OUT OF OR BASED UPON THIS AGREEMENT, THE LOAN DOCUMENTS OR ANY CONTEMPLATED TRANSACTION, INCLUDING CONTRACT, TORT, BREACH OF DUTY AND ALL OTHER CLAIMS. THIS WAIVER IS A MATERIAL INDUCEMENT FOR ALL PARTIES HERETO TO ENTER INTO THIS AGREEMENT. EACH PARTY HERETO HAS REVIEWED THIS WAIVER WITH ITS COUNSEL.

11 GENERAL PROVISIONS

11.1. Successors and Assigns.

(a) This Agreement binds and is for the benefit of the parties hereto and their respective successors and permitted assigns.

(b) No Credit Party may transfer, pledge or assign this Agreement or any other Loan Document or any rights or obligations hereunder or thereunder without the prior written consent of each Lender. Subject to Section 11.1(d), any Lender may at any time sell, transfer, assign or pledge this Agreement or any other Loan Document or any of its rights or obligations hereunder or thereunder, including with respect to any Term Loan (or any portion thereof), to any Eligible Transferee without Borrower's prior written consent, including to grant a participation in all or any part of, or any interest in, Lender's obligations, rights or benefits under this Agreement and the other Loan Documents, including with respect to any Term Loan (or any portion thereof) (any such sale, transfer, assignment, pledge or grant of a participation, a "**Lender Transfer**"); provided, however, that after the occurrence and during the continuance of an Event of Default, any Lender may make a Lender Transfer to any Person without Borrower's prior written consent; provided, further, that no Lender may make a Lender Transfer to a Competitor of Borrower without Borrower's prior written consent except after the occurrence and during the continuance of an Event of Default described in Section 7.1 or Section 7.5.

(c) In the case of a Lender Transfer in the form of a participation granted by any Lender to any third party, (i) such Lender's obligations under this Agreement shall remain unchanged, (ii) such Lender shall remain solely responsible to the other parties hereto for the performance of its obligations hereunder, (iii) Borrower shall continue to deal solely and directly with such Lender in connection with such Lender's rights and obligations under this Agreement and (iv) any agreement or instrument pursuant to which such Lender sells such participation shall

provide that such Lender shall retain the sole right to enforce this Agreement and to approve any amendment, modification, or other modification hereto, in each case subject to the terms and conditions of this Agreement. Borrower agrees that each participant shall be entitled to the benefits of Sections 2.5 and 2.6 (subject to the requirements and limitations therein, including the requirements under Section 2.6(d) (it being understood that the documentation required under Section 2.6(d) shall be delivered to the applicable Lender)) to the same extent as if it were a Person that had acquired its interest by assignment pursuant to clause (b) above; provided that, with respect to any participation, such participant shall not be entitled to receive any greater payment under Sections 2.5 or 2.6 than the applicable Lender (i.e., the party that participated the interest) would have been entitled to receive, except to the extent of any entitlement to receive a greater payment resulting from a Change in Law that occurs after such participant acquired the applicable participation.

(d) The Collateral Agent shall record any Lender Transfer in the Register. Each Lender shall provide Borrower and the Collateral Agent with written notice of a Lender Transfer delivered no later than five (5) Business Days prior to the date on which such Lender Transfer is consummated. If any Lender sells a participation, such Lender shall, acting solely for this purpose as a non-fiduciary agent of Borrower, maintain a register on which it enters the name and address of each participant and principal amounts (and stated interest) of each participant's interest in the Term Loan(s) or other obligations under the Loan Documents (the "Participant Register"); provided, however, that such Lender shall have no obligation to disclose all or any portion of the Participant Register (including the identity of any participant or any information relating to a participant's interest in any commitments, loans or its other obligations under any Loan Document) to any Person except to the extent that such disclosure is necessary to establish that such commitment, loan, letter of credit or other obligation is in registered form under Section 5f.103-1(c) or Proposed Section 1.163-5(b) of the Treasury Regulations (or, in each case, any amended or successor version). The entries in the Participant Register shall be conclusive absent manifest error, and the Collateral Agent and each Lender shall treat each Person whose name is recorded in the Participant Register as the owner of such participation for all purposes of this Agreement notwithstanding any notice to the contrary.

(e) Any attempted transfer, pledge or assignment of this Agreement or any other Loan Document or any rights or obligations hereunder or thereunder in violation of this Section 11.1 shall be null and void.

11.2. Indemnification.

(a) Borrower agrees to indemnify and hold harmless each of the Collateral Agent, Lenders and its and their respective Affiliates (and its or their respective successors and assigns) and each manager, member, partner, controlling Person, director, officer, employee, agent or sub-agent, advisor and affiliate thereof (each such Person, an "**Indemnified Person**") from and against any and all Indemnified Liabilities; provided, however, that (i) Borrower shall have no obligation to any Indemnified Person hereunder with respect to any Indemnified Liabilities to the extent such Indemnified Liabilities arise from the bad faith, gross negligence or willful misconduct of that Indemnified Person (or its Affiliates or controlling Persons or their respective directors, officers, managers, partners, members, agents, sub-agents or advisors), in each case, as determined by a final, non-appealable judgment of a court of competent jurisdiction, (ii) Borrower shall have no obligation to any Indemnified Person hereunder with respect to any Indemnified Liabilities if and to the extent such Indemnified Liabilities arise from a material breach of any obligation of such Indemnified Person hereunder, and (iii) Borrower shall have no obligation to any Indemnified Person hereunder with respect to any Indemnified Liabilities if and to the extent such Indemnified Liabilities arise from any claim by one Indemnified Person against another Indemnified Person that does not relate to any act or omission of any Credit Party, and (iv) no Credit Party shall be liable for any settlement of any claim or proceeding effected by any Indemnified Person without the prior written consent of such Credit Party (which consent shall not be unreasonably withheld, conditioned or delayed), but if settled with such consent or if there shall be a final judgment against an Indemnified Person, each of the Credit Parties shall, jointly and severally with each other Credit Parties, indemnify and hold harmless such Indemnified Person from and against any loss or liability by reason of such settlement or judgment in the manner set forth in this Agreement. This Section 11.2(a) shall not apply with respect to Taxes other than any Taxes that represent liabilities, obligations, losses, damages, penalties, claims, costs, expenses and disbursements arising from any non-Tax claim.

(b) To the extent permitted by Requirements of Law, no party to this Agreement shall assert, and each party to this Agreement hereby waives, any claim against any other party hereto (and its or their successors and assigns), and each manager, member, partner, controlling Person, director, officer, employee, agent or sub-agent, advisor and affiliate thereof, on any theory of liability, for special, indirect, consequential or punitive damages (as opposed to direct or actual damages) (whether or not the claim therefor is based on contract, tort or duty imposed by any applicable legal requirement) arising out of, in connection with, arising out of, as a result of, or in any way related to, this Agreement or any Loan Document or any agreement or instrument contemplated hereby or thereby or referred to herein or therein, the transactions contemplated hereby or thereby, the Term Loans or the use of the proceeds thereof or any act or omission or event occurring in connection therewith, and each party to this Agreement hereby waives, releases and agrees not to sue upon any such claim or any such damages, whether or not accrued and whether or not known or suspected to exist in its favor.

(c) Any action taken by any Credit Party under or with respect to any Loan Document, even if required under any Loan Document or at the request of the Collateral Agent or any Lender, shall be at the expense of such Credit Party, and neither the Collateral Agent nor any Secured Party shall be required under any Loan Document to reimburse any Credit Party or any Subsidiary of any Credit Party therefor except as expressly provided therein. In addition, and without limiting the generality of Section 2.4, Borrower agrees to pay or reimburse upon demand each of the Collateral Agent and Lenders (and their respective successors and assigns) and each of their respective Related Parties for any and all fees, expenses and disbursements of the kind or nature described in clause (ii) of the definition of "Lender Expenses" incurred by it.

11.3. Severability of Provisions. In case any provision in or obligation hereunder or under any other Loan Document shall be invalid, illegal or unenforceable in any jurisdiction, the validity, legality and enforceability of the remaining provisions or obligations, or of such provision or obligation in any other jurisdiction, shall not in any way be affected or impaired thereby.

11.4. Correction of Loan Documents. The Collateral Agent or Required Lenders may correct patent errors and fill in any blanks in the Loan Documents consistent with the agreement of the parties hereto so long as the Collateral Agent or Required Lenders, as applicable, provides the Credit Parties and the other parties hereto with written notice of such correction and allows the Credit Parties at least ten (10) days to object to such correction in writing delivered to the Collateral Agent and each Lender. In the event of such objection, such correction shall not be made except by an amendment to this Agreement in accordance with Section 11.5.

11.5. Amendments in Writing; Integration.

(a) No amendment, restatement or modification of any provision of this Agreement or any other Loan Document, or waiver, discharge or termination of any obligation hereunder or thereunder, no approval or consent hereunder or thereunder (including any consent to any departure by Borrower or any other Credit Party herefrom or therefrom), shall in any event be effective unless the same shall be in writing and signed by Borrower (on its own behalf and on behalf of each other Credit Party) and the Required Lenders; provided, however, that no such amendment, restatement, modification, waiver, discharge, termination, approval or consent shall, unless in writing and signed by the Collateral Agent and the Required Lenders, affect the rights or duties of, or any amounts payable to, the Collateral Agent under this Agreement or any other Loan Document. Any such waiver, approval or consent granted shall be limited to the specific circumstance expressly described in it, and shall not apply to any subsequent or other circumstance, whether similar or dissimilar, or give rise to, or evidence, any obligation or commitment to grant any further waiver, approval or consent.

(b) This Agreement and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements. All prior agreements, understandings, representations, warranties, and negotiations among the parties hereto about the subject matter of this Agreement and the Loan Documents merge into this Agreement and the Loan Documents.

11.6. Counterparts. This Agreement may be executed in any number of counterparts and by different parties on separate counterparts, each of which, when executed and delivered, is an original, and all taken together, constitute one Agreement.

11.7. Survival. All covenants, representations and warranties made in this Agreement continue in full force until this Agreement has terminated pursuant to its terms and all Obligations (other than inchoate indemnity obligations and any other obligations which, by their terms, are to survive the termination of this Agreement) have been paid in full and satisfied. The obligation of Borrower or any other the Credit Parties in Section 11.2 to indemnify Indemnified Persons shall survive until the statute of limitations with respect to such claim or cause of action shall have run.

11.8. Confidentiality. Any information regarding the Credit Parties and their Subsidiaries and their businesses provided to the Collateral Agent or any Lender by or on behalf of any Credit Party pursuant to the Loan Documents shall be deemed "Confidential Information"; provided, however, that Confidential Information does not include information that is either: (i) in the public domain or in the possession of the Collateral Agent, any Lender or any of their respective Affiliates or when disclosed to the Collateral Agent, any Lender or any of their respective Affiliates, or becomes part of the public domain after disclosure to the Collateral Agent, any Lender or any of their respective Affiliates, in each case, other than as a result of a breach by the Collateral Agent, any Lender or any of their respective Affiliates of the obligations under this Section 11.8; or (ii) disclosed to the Collateral Agent, any Lender or any of their respective Affiliates by a third party if the Collateral Agent, such Lender or such Affiliate, as applicable, does not know that the third party is prohibited from disclosing the information. Neither the Collateral Agent nor any Lender shall disclose any Confidential Information to a third party or use Confidential Information for any purpose other than the exercise of its rights and the performance of its duties or obligations under the Loan Documents. The foregoing in this Section 11.8 notwithstanding, the Collateral Agent and each Lender may disclose Confidential Information: (a) to any of its Subsidiaries or Affiliates; (b) to prospective transferees, purchasers or participants of any interest in the Credit Extensions (including, for the avoidance of doubt, in connection with any proposed Lender Transfer); (c) as required by law, regulation, subpoena, or other order, provided, that (x) prior to any disclosure under this clause (c), the Collateral Agent or such Lender, as applicable, agrees to endeavor to provide Borrower with prior written notice thereof and with respect to any law, regulation, subpoena or other order, to the extent that the Collateral Agent or such Lender is permitted to provide such prior notice to Borrower pursuant to the terms hereof, and (y) any disclosure under this clause (c) shall be limited solely to that portion of the Confidential Information as may be specifically compelled by such law, regulation, subpoena or other order; (d) to the extent requested by regulators having jurisdiction over the Collateral Agent or such Lender or as otherwise required in connection with the Collateral Agent's or such Lender's examination or audit by such regulators; (e) as the Collateral Agent or such Lender considers reasonably necessary in exercising remedies under the Loan Documents; (f) to third-party service providers of the Collateral Agent or such Lender; and (g) to any of the Collateral Agent's or such Lender's Related Parties; provided, however, that the third parties to which Confidential Information is disclosed pursuant to clauses (a), (b), (f) and (g) are bound by obligations of confidentiality and non-use that are no less restrictive than those contained herein.

The provisions of this Section 11.8 shall survive the termination of this Agreement.

11.9. Attorneys' Fees, Costs and Expenses. In any action or proceeding between any Credit Party and the Collateral Agent or any Lender arising out of or relating to the Loan Documents, the prevailing party shall be entitled to recover its reasonable attorneys' fees and other costs and expenses incurred, in addition to any other relief to which it may be entitled.

11.10. Right of Set-Off. In addition to any rights now or hereafter granted under Requirements of Law and not by way of limitation of any such rights, upon the occurrence of an Event of Default and at any time thereafter during the continuance of any Event of Default, each Lender is hereby authorized by each Credit Party at any time or from time to time, without prior notice to any Credit Party, any such notice being hereby expressly waived by Borrower (on its own behalf and on behalf of each other Credit Party), to set off and to appropriate and to apply any and all deposits (general or special, including Indebtedness evidenced by certificates of deposit, whether matured or unmatured, but not including trust accounts) and any other Indebtedness at any time held or owing by such Lender to or for the credit or the account of any Credit Party against and on account of the obligations and liabilities of any Credit Party to such Lender hereunder and under the other Loan Documents, including all claims of any nature or description arising out of or connected hereto or with any other Loan Document, irrespective of whether or not (a) the Collateral Agent or such Lender shall have made any demand hereunder or (b) the principal of or the interest on the Term Loans or any other amounts due hereunder shall have become due and payable pursuant to Section 2 and although such obligations and liabilities, or any of them, may be contingent or unmatured. Each Lender agrees promptly to notify Borrower and the Collateral Agent after any such set off and application made by such Lender; provided, that the failure to give such notice shall not affect the validity of such set off and application.

11.11. Marshalling; Payments Set Aside. Neither the Collateral Agent nor any Lender shall be under any obligation to marshal any assets in favor of any Credit Party or any other Person or against or in payment of any or all of the Obligations. To the extent that any Credit Party makes a payment or payments to any Lender, or the Collateral Agent or any Lender enforces any Liens or exercises its rights of setoff, and such payment or payments or the proceeds of such enforcement or setoff or any part thereof are subsequently invalidated, declared to be fraudulent or preferential, set aside or required to be repaid to a trustee, receiver or any other party under any bankruptcy law, any other state or federal law, common law or any equitable cause, then, to the extent of such recovery, the obligation or part thereof originally intended to be satisfied, and all Liens, rights and remedies therefor or related thereto, shall be revived and continued in full force and effect as if such payment or payments had not been made or such enforcement or setoff had not occurred.

11.12. Electronic Execution of Documents. The words "execution," "signed," "signature" and words of like import in any Loan Document shall be deemed to include electronic signatures or the keeping of records in electronic form, each of which shall be of the same legal effect, validity and enforceability as a manually executed signature or the use of a paper-based recordkeeping systems, as the case may be, to the extent and as provided for in any Requirements of Law, including any state law based on the Uniform Electronic Transactions Act.

11.13. Captions. Section headings herein are included herein for convenience of reference only and shall not constitute a part hereof for any other purpose or be given any substantive effect.

11.14. Construction of Agreement. The parties hereto mutually acknowledge that they and their respective attorneys have participated in the preparation and negotiation of this Agreement. In cases of uncertainty, this Agreement shall be construed without regard to which of the parties hereto caused the uncertainty to exist.

11.15. Third Parties. Nothing in this Agreement, whether express or implied, is intended to: (a) except as expressly provided in Section 11.2(a), confer any benefits, rights or remedies under or by reason of this Agreement on any Persons other than the express parties to it and their respective successors and permitted assigns; (b) relieve or discharge the obligation or liability of any Person not an express party to this Agreement; or (c) give any Person not an express party to this Agreement any right of subrogation or action against any party to this Agreement.

11.16. No Advisory or Fiduciary Duty. The Collateral Agent and each Lender may have economic interests that conflict with those of the Credit Parties. Each Credit Party agrees that nothing in the Loan Documents or otherwise will be deemed to create an advisory, fiduciary or agency relationship or fiduciary or other implied duty between any Lender or the Collateral Agent, on the one hand, and such Credit Party, its Subsidiaries, and any of their respective stockholders or affiliates, on the other hand. Each Credit Party acknowledges and agrees that (i) the transactions contemplated by the Loan Documents are arm's-length commercial transactions between each Lender and the Collateral Agent, on the one hand, and such Credit Party, its Subsidiaries and their respective affiliates, on the other hand, (ii) in connection therewith and with the process leading to such transaction, the Collateral Agent and each Lender is acting solely as a principal and not the advisor, agent or fiduciary of such Credit Party, its Subsidiaries or their respective affiliates, management, stockholders, creditors or any other Person, (iii) Neither the Collateral Agent nor any Lender has assumed an advisory or fiduciary responsibility in favor of any Credit Party, its Subsidiaries or their respective affiliates with respect to the transactions contemplated hereby or the process leading thereto (irrespective of whether the Collateral Agent or any Lender or any of their respective affiliates has advised or is currently advising such Credit Party, its Subsidiaries or their respective affiliates on other matters) or any other obligation to such Credit Party, its Subsidiaries or their respective affiliates except the obligations expressly set forth in the Loan Documents and (iv) each Credit Party, its Subsidiaries and their respective affiliates have consulted their own legal and financial advisors to the extent each deemed appropriate. Each Credit Party further acknowledges and agrees that it is responsible for making its own independent judgment with respect to such transactions and the process leading thereto. Each Credit Party agrees that it will not claim that the Collateral Agent or any Lender has rendered advisory services of any nature or respect, or owes a fiduciary or similar duty to such Credit Party, its Subsidiaries or their respective affiliates in connection with such transaction or the process leading thereto.

12 COLLATERAL AGENT

12.1. Appointment and Authority. Each of the Lenders hereby irrevocably appoints BioPharma Credit PLC to act on its behalf as the Collateral Agent hereunder and under the other Loan Documents and authorizes the Collateral Agent to take such actions on its behalf and to exercise such powers as are delegated to the Collateral Agent by the terms hereof or thereof, together with such actions and powers as are reasonably incidental thereto. Except for the first two (2) sentences of Section 12.6 and the penultimate paragraph of Section 12.8, the provisions of this Section 12 are solely for the benefit of the Collateral Agent and the Lenders, and neither Borrower nor any other Credit Party shall have rights as a third party beneficiary of any of such provisions. Subject to Section 12.8 and Section 11.5, any action required or permitted to be taken by the Collateral Agent hereunder shall be taken with the prior approval of the Required Lenders.

12.2. Rights as a Lender. The Person serving as the Collateral Agent hereunder shall have the same rights and powers in its capacity as a Lender as any other Lender and may exercise the same as though it were not the Collateral Agent and the term "Lender" or "Lenders" shall, unless otherwise expressly indicated or unless the context otherwise requires, include the Person serving as the Collateral Agent hereunder in its individual capacity. Such Person and its Affiliates may lend money to, own securities of, act as the financial advisor or in any other advisory capacity for and generally engage in any kind of business with Borrower or any Subsidiary or other Affiliate thereof as if such Person were not the Collateral Agent hereunder and without any duty to account therefor to the Lenders.

12.3. Exculpatory Provisions.

(a) The Collateral Agent shall not have any duties or obligations to the Lenders except those expressly set forth herein and in the other Loan Documents to which it is a party. Without limiting the generality of the foregoing, with respect to the Lenders, the Collateral Agent:

(i) shall not be subject to any fiduciary or other implied duties, regardless of whether a Default or Event of Default has occurred and is continuing;

(ii) shall not have any duty to take any discretionary action or exercise any discretionary powers, except discretionary rights and powers expressly contemplated hereby or by the other Loan Documents to which it is a party that the Collateral Agent is required to exercise as directed in writing by the Required Lenders (or such other number or percentage of the Lenders as shall be expressly provided for herein or in such other Loan Documents), provided that the Collateral Agent shall not be required to take any action that, in its opinion or the opinion of its counsel, may expose the Collateral Agent to liability or that is contrary to any Loan Document or Requirements of Law; and

(iii) shall not, except as expressly set forth herein and in the other Loan Documents to which it is a party, have any duty to disclose, and shall not be liable for the failure to disclose, any information relating to Borrower or any of its Affiliates that is communicated to or obtained by the Person serving as the Collateral Agent or any of its Affiliates in any capacity.

(b) The Collateral Agent shall not be liable for any action taken or not taken by it (i) with the consent or at the request of the Required Lenders (or such other number or percentage of the Lenders as shall be necessary, or as the Collateral Agent shall believe in good faith shall be necessary, under the circumstances as provided in Section 11.5) or (ii) in the absence of its own gross negligence or willful misconduct as determined by a court of competent jurisdiction by final and nonappealable judgment. The Collateral Agent shall be deemed not to have knowledge of any Default or Event of Default unless and until notice describing such Default or Event of Default is given to the Collateral Agent in writing by Borrower or a Lender.

(c) The Collateral Agent shall not be responsible for or have any duty to ascertain or inquire into (i) any statement, warranty or representation made in or in connection with this Agreement or any other Loan Document, (ii) the contents of any certificate, report or other document delivered hereunder or thereunder or in connection herewith or therewith, (iii) the performance or observance of any of the covenants, agreements or other terms or conditions set forth herein or therein or the occurrence of any Default or Event of Default, (iv) the validity, enforceability, effectiveness or genuineness of this Agreement, any other Loan Document or any other agreement, instrument or document or (v) the satisfaction of any condition set forth in Section 3 or elsewhere herein, other than to confirm receipt of items expressly required to be delivered to the Collateral Agent.

12.4. Reliance by Collateral Agent. The Collateral Agent shall be entitled to rely upon, and shall not incur any liability for relying upon, any notice, request, certificate, consent, statement, instrument, document or other writing (including any electronic message, internet or intranet website posting or other distribution) believed by it to be genuine and to have been signed, sent or otherwise authenticated by the proper Person. The Collateral Agent also may rely upon any statement made to it orally or by telephone and believed by it to have been made by the proper Person, and shall not incur any liability for relying thereon. The Collateral Agent may consult with legal counsel (who may be counsel for Borrower), independent accountants and other experts selected by it, and shall not be liable for any action taken or not taken by it in accordance with the advice of any such counsel, accountants or experts.

12.5. Delegation of Duties. The Collateral Agent may perform any and all of its duties and exercise its rights and powers hereunder or under any other Loan Document by or through any one or more sub-agents appointed by the Collateral Agent. The Collateral Agent and any such sub-agent may perform any and all of its duties and exercise its rights and powers by or through their respective Related Parties. The exculpatory provisions of this Section 12 shall apply to any such sub-agent and to the Related Parties of the Collateral Agent and any such sub-agent. The Collateral Agent shall not be responsible for the negligence or misconduct of any sub-agent except to the extent that a court of competent jurisdiction determines in a final and nonappealable judgment that the Collateral Agent acted with gross negligence or willful misconduct in the selection of such sub-agent.

12.6. Resignation of Collateral Agent. The Collateral Agent may at any time give notice of its resignation to the Lenders and Borrower. Upon the receipt of any such notice of resignation, the Required Lenders shall have the right, in consultation with Borrower so long as no Default or Event of Default has occurred and is continuing, to appoint a successor. If no successor shall have been so appointed by the Required Lenders and shall have accepted such appointment within thirty (30) days after the retiring Collateral Agent gives notice of its resignation, then the retiring Collateral Agent may, on behalf of the Lenders, appoint a successor Collateral Agent; provided that, whether or not a successor has been appointed or has accepted such appointment, such resignation shall become effective upon delivery of the notice thereof. Upon the acceptance of a successor's appointment as Collateral Agent hereunder, such successor shall succeed to and become vested with all of the rights, powers, privileges and duties of the retiring (or retired) Collateral Agent, and the retiring Collateral Agent shall be discharged from all of its duties and obligations under the Loan Documents (if not already discharged therefrom as provided above in this Section 12.6). After the retiring Collateral Agent's resignation, the provisions of this Section 12 and Section 10 shall continue in effect for the benefit of such retiring Collateral Agent, its sub-agents and their respective Related Parties in respect of any actions taken or omitted to be taken by any of them while the retiring Collateral Agent was acting as Collateral Agent. Upon any resignation by the Collateral Agent, all payments, communications and determinations provided to be made by, to or through the Collateral Agent shall instead be made by, to or through each Lender directly, until such time as a Person accepts an appointment as Collateral Agent in accordance with this Section 12.6.

12.7. Non-Reliance on Collateral Agent and Other Lenders. Each Lender acknowledges that it has, independently and without reliance upon the Collateral Agent or any other Lender or any of their respective Related Parties and based on such documents and information as it has deemed appropriate, made its own credit analysis and decision to enter into this Agreement and make Credit Extensions hereunder. Each Lender also acknowledges that it will, independently and without reliance upon the Collateral Agent or any other Lender or any of their respective Related Parties and based on such documents and information as it shall from time to time deem appropriate, continue to make its own decisions in taking or not taking action under or based upon this Agreement, any other Loan Document or any related agreement or any document furnished hereunder or thereunder.

12.8. Collateral and Guaranty Matters. Each Lender agrees that any action taken by the Collateral Agent or the Required Lenders in accordance with the provisions of this Agreement or of the other Loan Documents, and the exercise by the Collateral Agent or Required Lenders of the powers set forth herein or therein, together with such other powers as are reasonably incidental thereto, shall be authorized and binding upon all of the Lenders. Without limiting the generality of the foregoing, the Lenders irrevocably authorize the Collateral Agent, at its option and in its discretion, and the Collateral Agent agrees:

(a) to release any Lien on any property granted to or held by the Collateral Agent under any Collateral Document (i) upon payment in full of the Obligations (other than unasserted inchoate indemnity obligations), (ii) that is sold, transferred, disposed or to be sold, transferred, disposed as part of or in connection with any sale, transfer or other disposition (other than any sale to a Credit Party) permitted hereunder, (iii) subject to Section 11.5, if approved, authorized or ratified in writing by the Required Lenders, or (iv) to the extent such property is owned by a Guarantor upon the release of such Guarantor from its obligations under the Loan Documents pursuant to clause (c) below;

(b) to subordinate any Lien on any property granted to or held by the Collateral Agent under any Loan Document to the holder of any Lien on such property that is permitted by clause (d), (i), (j), (m), (n) and (r) of the definition of "Permitted Liens" (solely with respect to modifications, replacements, extensions or renewals of Liens permitted under clause (d), (i), (j), (m) and (n) of the definition of "Permitted Liens");

(c) to release any Guarantor from its obligations under the Security Agreement if such Person ceases to be a Subsidiary as a result of a transaction permitted hereunder or upon payment in full of the Obligations (other than unasserted inchoate indemnity obligations);

(d) to enter into non-disturbance and similar agreements in connection with the licensing of Intellectual Property permitted pursuant to the terms of this Agreement; and

(e) to enter into a subordination, intercreditor, or other similar agreement with respect to any Indebtedness that constitutes Subordinated Debt to the extent such Subordinated Debt is permitted under the definition of "Permitted Indebtedness".

Upon request by the Collateral Agent at any time the Required Lenders will confirm in writing the Collateral Agent's authority to release or subordinate its interest in particular types or items of property, or to release any Guarantor from its obligations under the Security Agreement pursuant to this Section 12.8.

In each case as specified in this Section 12.8, the Collateral Agent will (and each Lender irrevocably authorizes the Collateral Agent to), at Borrower's expense, execute and deliver to the applicable Credit Party such documents as such Credit Party may reasonably request (i) to evidence the release or subordination of such item of Collateral from the Liens and security interests granted under the Collateral Documents, (ii) to enter into non-disturbance or similar agreements in connection with the licensing of Intellectual Property, (iii) to enter into a subordination, intercreditor, or other similar agreement with respect to any Indebtedness that constitutes Subordinated Debt to the extent such Subordinated Debt is permitted under the definition of "Permitted Indebtedness" or (iv) to evidence the release of any Guarantor from its obligations under the Security Agreement, in each case in accordance with the terms of the Loan Documents and this Section 12.8 and in form and substance reasonably acceptable to the Collateral Agent.

Without limiting the generality of Section 12.10 below, the Collateral Agent shall deliver to the Lenders notice of any action taken by it under this Section 12.8 promptly after the taking thereof; provided that delivery of or failure to deliver any such notice shall not affect the Collateral Agent's rights, powers, privileges and protections under this Section 12.

12.9. Reimbursement by Lenders. To the extent that Borrower for any reason fails to indefeasibly pay any amount required under Section 2.4 to be paid by it to the Collateral Agent (or any sub-agent thereof) or any Related Party of any of the foregoing, each Lender severally agrees to pay to the Collateral Agent (or any such sub-agent) or such Related Party, as the case may be, such Lender's *pro rata* share (based upon the percentages as used in determining the Required Lenders as of the time that the applicable unreimbursed expense or indemnity payment is sought) of such unpaid amount; provided that the unreimbursed expense or indemnified loss, damage, liability or related expense, as the case may be, was incurred by or asserted against the Collateral Agent (or any such sub-agent) in its capacity as such or against any Related Party of any of the foregoing acting for the Collateral Agent (or any sub-agent) in connection with such capacity.

12.10. Notices and Items to Lenders. The Collateral Agent shall deliver to the Lenders each notice, report, statement, approval, direction, consent, exemption, authorization, waiver, certificate, filing or other item received by it pursuant to this Agreement or any other Loan Document (including any item received by it pursuant to Section 3 or set forth on Schedule 5.14 of the Disclosure Letter); provided, that any delivery of or failure to deliver any such notice, report, statement, approval, direction, consent, exemption, authorization, waiver, certificate, filing or item shall not otherwise alter or effect the rights of the Lenders or the Collateral Agent under this Agreement or any

other Loan Document or the validity of such item. In addition, to the extent the Collateral Agent or the Required Lenders deliver any notices, approvals, authorizations, directions, consents or waivers to Borrower pursuant to this Agreement or any other Loan Document, the Collateral Agent or the Required Lenders, as applicable, will also deliver such notice, approval, authorization, direction, consent or waiver to the other Lenders on or about the same time such notice, approval, authorization, direction, consent or waiver is provided to Borrower; provided, that the delivery of or failure to deliver such notice, approval, authorization, direction, consent or waiver to the other Lenders shall not in any way effect the obligations of Borrower, or the rights of the Collateral Agent or the Required Lenders, in respect of such notice, approval, authorization, direction, consent or waiver or the validity thereof.

13 DEFINITIONS

13.1. Definitions. For the purposes of and as used in the Loan Documents: (a) references to any Person include its successors and assigns and, in the case of any Governmental Authority, any Person succeeding to its functions and capacities; (b) except as the context otherwise requires (including to the extent otherwise expressly provided in any Loan Document), (i) references to any law, statute, treaty, order, policy, rule or regulation include any amendments, supplements and successors thereto and (ii) references to any contract, agreement, instrument or other document include any amendments, restatements, supplements or modifications thereto or thereof from time to time to the extent permitted by the provisions thereof; (c) the word "shall" is mandatory; (d) the word "may" is permissive; (e) the word "or" has the inclusive meaning represented by the phrase "and/or"; (f) the words "include", "includes" and "including" are not limiting; (g) the singular includes the plural and the plural includes the singular; (h) numbers denoting amounts that are set off in parentheses are negative unless the context dictates otherwise; (i) each authorization herein shall be deemed irrevocable and coupled with an interest; (j) all accounting terms shall be interpreted, and all determinations relating thereto shall be made, in accordance with Applicable Accounting Standards; (k) references to any time of day shall be to New York time; (l) the words "herein", "hereof", "hereby", "hereto" and "hereunder" refer to this Agreement as a whole; and (m) unless otherwise expressly provided, references to specific sections, articles, clauses, sub-clauses, annexes and exhibits are to this Agreement and references to specific schedules are to the Disclosure Letter. As used in this Agreement, the following capitalized terms have the following meanings:

"**Account**" means any "account" as defined in the Code with such additions to such term as may hereafter be made, and includes all accounts receivable, book debts, and other sums owing to Credit Parties.

"**Account Debtor**" means any "account debtor" as defined in the Code with such additions to such term as may hereafter be made.

"**Acquisition**" means (a) any Stock Acquisition, or (b) any Asset Acquisition.

"**Additional Commitment Consideration**" is defined in Section 2.7(a).

"**Additional Consideration**" is defined in Section 2.7(b).

"**Additional Loan Consideration**" is defined in Section 2.7(b).

"**Adverse Proceeding**" means any action, suit, proceeding, hearing (whether administrative, judicial or otherwise), governmental investigation or arbitration (whether or not purportedly on behalf of any Credit Party or any of its Subsidiaries) at law or in equity, or before or by any Governmental Authority, domestic or foreign (including any Environmental Claims), whether pending or, to the Knowledge of Borrower, threatened against or adversely affecting any Credit Party or any of its Subsidiaries or any property of any Credit Party or any of its Subsidiaries.

"**Affiliate**" means, with respect to any Person, each other Person that owns or controls directly or indirectly the Person, any Person that controls or is controlled by or is under common control with the Person, and each of that Person's senior executive officers, directors, partners and, for any Person that is a limited liability company or limited liability partnership, that Person's managers and members. As used in this definition, "control" means (a) direct or indirect beneficial ownership of at least fifty percent (50%) (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) of the voting share capital or other equity interest in a Person or (b) the power to direct or cause the direction of the management of such Person by contract or otherwise. In no event shall the Collateral Agent or any Lender be deemed to be an Affiliate of Borrower or any of its Subsidiaries.

"**Agreement**" is defined in the preamble hereof.

"**Anti-Money Laundering Laws**" is defined in Section 4.18(b).

"**Applicable Accounting Standards**" means with respect to Borrower and its Subsidiaries, generally accepted accounting principles in the United States as set forth in the opinions and pronouncements of the Accounting Principles Board of the American Institute of Certified Public Accountants and statements and pronouncements of the Financial Accounting Standards Board or in such other statements by such other Person as may be approved by a significant segment of the accounting profession, which are applicable to the circumstances as of the date of determination, consistently applied.

"**Applicable Percentage**" means, with respect to each Lender at any time of determination, the percentage equal to a fraction, the numerator of which is the amount of such Lender's Term Loan Commitment and the denominator of which is an amount equal to the aggregate principal of the Term Loans at such time.

"**Asset Acquisition**" means, with respect to Borrower or any of its Subsidiaries, any purchase, in-license or other acquisition of any properties or assets of any other Person (including any purchase or other acquisition of any business unit, line of business or division of such Person). For the avoidance of doubt, "Asset Acquisition" includes any co-promotion or co-marketing arrangement pursuant to which Borrower or any Subsidiary acquires rights to promote or market the products of another Person.

"**Bankruptcy Code**" means Title 11 of the United States Code entitled "Bankruptcy," as now and hereafter in effect, or any successor statute.

"**Blocked Person**" an individual or entity that is, or is owned or controlled by individuals or entities that are: (i) the subject or target of any sanctions administered or enforced by the U.S. Department of the Treasury's Office of Foreign Assets Control ("**OFAC**"), the U.S. Department of State, the United Nations Security Council, the European Union, Her Majesty's Treasury or other relevant sanctions authority (collectively, "**Sanctions**"), or (ii) located, organized or resident in a country or territory that is the subject of Sanctions, including currently, Crimea, Cuba, Iran, North Korea, and Syria.

"**Board of Directors**" means, with respect to any Person, (i) in the case of any corporation, the board of directors of such Person, (ii) in the case of any limited liability company, the board of managers of such Person, or if there is none, the Board of Directors of the managing member of such Person, (iii) in the case of any partnership, the Board of Directors of the general partner of such Person and (iv) in any other case, the functional equivalent of the foregoing.

"**Board of Governors**" means the Board of Governors of the United States Federal Reserve System, or any successor thereto.

"**Books**" means all books and records including ledgers, records regarding a Credit Party's assets or liabilities, the Collateral, business operations or financial condition, and all computer programs or storage or any equipment containing such information.

"**Borrower**" is defined in the preamble hereof.

"**Borrowing Resolutions**" means, with respect to any Person, those resolutions adopted by such Person's Board of Directors and delivered by such Person to the Collateral Agent pursuant to Section 3.1 approving the Loan Documents to which such Person is a party and the transactions contemplated thereby (including the Term Loan), together with a certificate executed by its Secretary on behalf of such Person certifying that (a) such Person has the authority to execute, deliver, and perform its obligations under each of the Loan Documents to which it is a party, (b) that attached as Exhibit A to such certificate is a true, correct, and complete copy of the resolutions then in full force

and effect authorizing and ratifying the execution, delivery, and performance by such Person of the Loan Documents to which it is a party, (c) the name(s) and title(s) of the officers of such Person authorized to execute the Loan Documents to which such Person is a party on behalf of such Person, together with a sample of the true signature(s) of such Person(s), and (d) that the Collateral Agent and each Lender may conclusively rely on such certificate with respect to the authority of such officers unless and until such Person shall have delivered to the Collateral Agent a further certificate canceling or amending such prior certificate.

"**Business Day**" means any day that is not a Saturday or a Sunday or a day on which banks are authorized or required to be closed in New York, New York, London or the Cayman Islands.

"**Capital Lease**" means, as applied to any Person, any lease of any property by that Person as lessee which, in accordance with Applicable Accounting Standards, is required to be accounted for as a capital lease on the balance sheet of that Person.

"**Cash Equivalents**" means

(a) securities issued or directly and fully guaranteed or insured by the United States government or any agency or instrumentality of the United States government or by the government of any other member country of O.E.C.D. (provided that the full faith and credit of the United States or such other member country of O.E.C.D., as applicable, is pledged in support of those securities), in each case, having maturities of not more than two (2) years from the date of acquisition;

(b) certificates of deposit, time deposits with maturities of one year or less from the date of acquisition, bankers' acceptances with maturities not exceeding one year and overnight bank deposits and demand deposits, in each case, with any commercial bank having (i) capital and surplus in excess of $500,000,000 in the case of U.S. banks or (ii) capital and surplus in excess of $100,000,000 (or the U.S. dollar equivalent as of the date of determination) in the case of non-U.S. banks;

(c) commercial paper or marketable short-term money market or readily marketable direct obligations and similar securities having one of the two highest ratings obtainable from Moody's Investors Services, Inc. or S&P Global Ratings and, in each case, maturing within two (2) years after the date of acquisition;

(d) repurchase obligations with a term of not more than seven (7) days for underlying securities of the types described in clauses (a) and (c) above entered into with any financial institution meeting the qualifications specified in clause (b) above;

(e) investment funds investing ninety-five percent (95.0%) of their assets in securities of the types described in clauses (a) through (d) above and clause (f) below;

(f) investments in money market funds rated "AAA" (or the equivalent thereof) or better by S&P Global Ratings or "Aaa" (or the equivalent thereof) or better by Moody's Investors Services, Inc. (or, if at any time neither Moody's Investors Services, Inc. nor S&P Global Ratings shall be rating such obligations, an equivalent rating from another rating agency) and that have portfolio assets of at least $1,000,000,000; and

(g) other investments in accordance with the Borrower's investment policy as of the Tranche A Closing Date or otherwise approved in writing by the Collateral Agent.

"**Change in Control**" means: (a) a transaction or series of transactions (including any merger or consolidation with Borrower) in which any "person" or "group" (within the meaning of Section 13(d) and 14(d)(2) of the Exchange Act, but excluding any employee benefit plan of such Person or its Subsidiaries, and any Person acting in its capacity as trustee, agent or other fiduciary or administrator of any such plan) is or becomes the "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of a majority of shares of the then outstanding capital stock of Borrower ordinarily entitled to vote in the election of directors; (b) a sale of all or substantially all of the consolidated assets of Borrower and its Subsidiaries in one transaction or a series of transactions (whether by way of merger, stock purchase, asset purchase or otherwise); or (c) a merger or consolidation involving Borrower in which Borrower is not the surviving Person.

"**Change in Law**" means the occurrence, after the date of this Agreement, of any of the following: (a) the adoption or taking into effect of any law, treaty, order, policy, rule or regulation, (b) any change in any law, treaty, order, policy, rule or regulation or in the administration, interpretation or application thereof by any Governmental Authority or (c) the making or issuance of any request, guideline or directive (whether or not having the force of law) by any Governmental Authority; provided that notwithstanding anything herein to the contrary, (x) the Dodd-Frank Wall Street Reform and Consumer Protection Act and all requests, rules, guidelines or directives thereunder or issued in connection therewith and (y) all requests, rules, guidelines or directives promulgated by the Bank for International Settlements, the Basel Committee on Banking Supervision (or any successor or similar authority) or the United States or foreign regulatory authorities, in each case pursuant to Basel III, shall be deemed to be a "Change in Law", regardless of the date enacted, adopted or issued.

"**Closing Date**" means the Tranche A Closing Date or the Tranche B Closing Date, as applicable.

"**Code**" means the Uniform Commercial Code, as the same may, from time to time, be enacted and in effect in the State of New York; provided, that, to the extent that the Code is used to define any term herein or in any Loan Document and such term is defined differently in different Articles of the Code, the definition of such term contained in Article 9 of the Code shall govern; provided, further, that in the event that, by reason of mandatory provisions of law, any or all of the attachment, perfection, or priority of, or remedies with respect to, the Collateral Agent's Lien, for the benefit of Lenders and the other Secured Parties, on any Collateral is governed by the Uniform Commercial Code in effect in a jurisdiction other than the State of New York, the term "Code" shall mean the Uniform Commercial Code as enacted and in effect in such other jurisdiction solely for purposes of the provisions thereof relating to such attachment, perfection, priority, or remedies and for purposes of definitions relating to such provisions.

"**Collateral**" means, collectively, "Collateral" (as such term is defined in the Security Agreement) and all other property of whatever kind and nature subject or purported to be subject from time to time to a Lien under any Collateral Document, but in any event excluding all Excluded Property.

"**Collateral Account**" means any Deposit Account of a Credit Party maintained with a bank or other depository or financial institution located in the United States, any Securities Account of a Credit Party maintained with a securities intermediary located in the United States, or any Commodity Account of a Credit Party maintained with a commodity intermediary located in the United States, in each case, other than an Excluded Account.

"**Collateral Documents**" means the Security Agreement, the Control Agreements, the IP Agreements, any Mortgages and all other instruments, documents and agreements delivered by any Credit Party pursuant to this Agreement or any of the other Loan Documents, in each case, in order to grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, or perfect a Lien on any Collateral as security for the Obligations, and all amendments, restatements, modifications or supplements thereof or thereto.

"**Commodity Account**" means any "commodity account" as defined in the Code with such additions to such term as may hereafter be made.

"**Company IP**" means any and all of the following, as they exist in and throughout the Territory: (a) Current Company IP; (b) improvements, continuations, continuations-in-part, divisions, provisionals or any substitute applications, any patent issued with respect to any of the Current Company IP, any patent right claiming the composition of matter of, or the method of making or using, any Product in the Territory, any reissue, reexamination, renewal or patent term extension or adjustment (including any supplementary protection certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent; (c) trade secrets or trade secret rights, including any rights to unpatented inventions, know-how, show-how, operating manuals, confidential or proprietary information, research in progress, algorithms, data, databases, data collections, designs, processes, procedures, methods, protocols, materials, formulae, drawings, schematics, blueprints, flow charts, models, strategies, prototypes, techniques, and the results of experimentation and testing, including samples, in each case, as specifically related to any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory; (d) any and all IP Ancillary Rights specifically relating to any of the foregoing; and (e) regulatory filings, submissions and approvals related to any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory and all data provided in any of the foregoing.

"**Compliance Certificate**" means that certain certificate in the form attached hereto as Exhibit E.

"**Competing Product**" means a product marketed for use in the treatment of sickle cell disease that is indicated broadly for the treatment of sickle cell patients and not exclusively for the treatment or prevention of vaso-occlusive crises or other sequelae of sickle cell disease.

"**Competitor**" means, at any time of determination, any Person that is an operating company directly and primarily engaged in the same or substantially the same line of business as Borrower and its Subsidiaries as of such time.

"**Connection Income Taxes**" means Other Connection Taxes that are imposed on or measured by net income (however denominated) or that are franchise Taxes or branch profits Taxes.

"**Contingent Obligation**" means, for any Person, any direct or indirect liability, contingent or not, of that Person for (a) any indebtedness, lease, dividend, letter of credit or other obligation of another Person directly or indirectly guaranteed, endorsed, co-made, discounted or sold with recourse by that Person, or for which that Person is directly or indirectly liable; (b) any obligation for undrawn letters of credit for the account of that Person; or (c) any obligation of that Person to pay an earn-out, milestone payment or similar contingent payment or deferred compensation to a counterparty incurred or created in connection with an Acquisition, Transfer or Investment or otherwise in connection with any collaboration, development or similar arrangement, excluding any obligation of that Person to pay deferred consideration or contingent purchase price described in clause (b) of the definition of "Indebtedness" but including, with respect to any purchase price holdback in respect of a portion of the purchase price of an asset, property, service or right sold to that Person to satisfy unperformed obligations of the seller of such asset, property, service or right, any obligation of that Person to pay such seller the excess of such holdback over such obligations of such seller. The amount of a Contingent Obligation is the stated or determined amount of the primary obligation for which the Contingent Obligation is made or, if not determinable, the maximum reasonably anticipated liability for it reasonably determined by such Person in good faith; but the amount may not exceed the maximum of the obligations under any guarantee or other support arrangement.

"**Control Agreement**" means, with respect to any Credit Party, any control agreement entered into among such Credit Party, the Collateral Agent and, in the case of a Deposit Account, the bank or other depository or financial institution located in the United States at which such Credit Party maintains such Deposit Account, or, in the case of a Securities Account or a Commodity Account, the securities intermediary or commodity intermediary located in the United States at which such Credit Party maintain such Securities Account or Commodities Account, in either case, pursuant to which the Collateral Agent obtains control (within the meaning of the Code) over such Collateral Account.

"**Copyrights**" means any and all copyright rights, copyright applications, copyright registrations and like protections in each work of authorship and derivative work thereof, whether published or unpublished and whether or not the same also constitutes a trade secret (and all related IP Ancillary Rights).

"**Credit Party**" means Borrower and each Guarantor.

"**Credit Extension**" means any Term Loan or any other extension of credit by any Lender for Borrower's benefit pursuant to this Agreement.

"**CSA**" is defined in Section 4.19(c).

"**Current Company IP**" is defined in Section 4.6(c).

"**Current Company IP Agreement**" means the Amended and Restated License Agreement by and between Borrower and the Regents of the University of California, dated July 20, 2016.

"**Data Protection Laws**" means any and all foreign or domestic, statutes, ordinances, orders, rules, regulations, judgments, Governmental Approvals, or any other requirements of Governmental Authorities relating to the privacy, security, or confidentiality of personal data (including individually identifiable information) and other sensitive information, including HIPAA, Section 5 of the Federal Trade Commission Act (15 U.S.C. § 45), and GDPR.

"**DEA**" means the United States Drug Enforcement Administration.

"**DEA Laws**" means all applicable statutes (including the CSA), rules, regulations and orders implemented, administered, enforced or issued by DEA (and any foreign or United States state equivalent).

"**Default**" means any breach of or default under any term, provision, condition, covenant or agreement contained in this Agreement or any other Loan Document or any other event, in each case that, with the giving of notice or the lapse of time or both, would constitute an Event of Default.

"**Deposit Account**" means any "deposit account" as defined in the Code with such additions to such term as may hereafter be made.

"**Disclosure Letter**" means the disclosure letter, dated the Effective Date, delivered by the Credit Parties to the Collateral Agent, as updated on the Closing Date (if required and as permitted).

"**Dollars**," "**dollars**" or use of the sign "**$**" means only lawful money of the United States and not any other currency, regardless of whether that currency uses the "$" sign to denote its currency or may be readily converted into lawful money of the United States.

"**Effective Date**" is defined in the preamble hereof.

"**Eligible Transferee**" means and includes a commercial bank, an insurance company, a finance company, a financial institution, any investment fund that invests in loans or any other institutional "accredited investor" (as defined in Regulation D of the Securities Act) that is principally in the business of managing investments or holding assets for investment purposes; provided, that any such Eligible Transferee (other than any Affiliate of BioPharma Credit PLC or BioPharma Credit Investments V (Master) LP) shall (i) have assets under management of no less than $1,000,000,000, (ii) have a rating of BBB or higher from S&P Global Ratings and a rating of Baa2 or higher from Moody's Investors Services, Inc. at the date it becomes a Lender and (iii) shall be capable of fulfilling of the assigning Lender's obligations (including funding obligations with respect to the Tranche B Loan, if applicable) hereunder.

"**Environmental Claim**" means any investigation, notice, notice of violation, claim, action, suit, proceeding, demand, abatement order or other order or directive (conditional or otherwise), by any Governmental Authority or any other Person, arising (i) pursuant to or in connection with any actual or alleged violation of any Environmental Law; (ii) in connection with any Hazardous Material or any actual or alleged Hazardous Materials Activity; or (iii) in connection with any actual or alleged damage, injury, threat or harm to health, safety, natural resources or the environment.

"**Environmental Laws**" means any and all current or future, foreign or domestic, statutes, ordinances, orders, rules, regulations, judgments, Governmental Approvals, or any other requirements of Governmental Authorities relating to (i) environmental matters, including those relating to any Hazardous Materials Activity; (ii) the generation, use, storage, transportation or disposal of Hazardous Materials; or (iii) occupational safety and health, industrial hygiene, land use or the protection of human, plant or animal health or welfare, in each case, in any manner applicable to any Credit Party or any of its Subsidiaries or any Facility.

"**Equity Interests**" means, with respect to any Person, any and all shares, interests, participations or other equivalents (however designated) of capital stock of a corporation, any and all equivalent ownership interests in such Person (other than a corporation), including partnership interests and membership interests, and any and all warrants, rights or options to purchase or other arrangements or rights to acquire (by purchase, conversion, dividend, distribution or otherwise) any of the foregoing (and all other rights, powers, privileges, interests, claims and other property in any manner arising therefrom or relating thereto).

"**ERISA**" means the Employee Retirement Income Security Act of 1974, and its regulations.

"**ERISA Affiliate**" means, with respect to any Person, any trade or business (whether or not incorporated) that, together with such Person, is treated as a single employer under Section 414(b) or (c) of the IRC or, solely for purposes of Section 302 of ERISA or Section 412 of the IRC, Section 412(m) or (o) of the IRC.

"**ERISA Event**" means (a) any "reportable event," as defined in Section 4043 of ERISA or the regulations issued thereunder, with respect to a Plan (other than an event for which the 30-day notice period is waived by regulation); (b) with respect to a Plan, the failure by Borrower or its Subsidiaries or their ERISA Affiliates to satisfy the minimum funding standard of Section 412 of the IRC and Section 302 of ERISA, whether or not waived; (c) the failure by Borrower or its Subsidiaries or their ERISA Affiliates to make by its due date a required installment under Section 430(j) of the IRC with respect to any Plan or to make any required contribution to a Multiemployer Plan; (d) the filing pursuant to Section 412(c) of the IRC or Section 302(c) of ERISA of an application for a waiver of the minimum funding standard with respect to any Plan; (e) the incurrence by Borrower or any of its ERISA Affiliates of any liability under Title IV of ERISA with respect to the termination of any Plan; (f) the receipt by Borrower or its Subsidiaries or any of their respective ERISA Affiliates from the Pension Benefit Guaranty Corporation (referred to and defined in ERISA) or a plan administrator of any notice relating to the intention to terminate any Plan or Plans under Section 4041 or 4041A of ERISA or to appoint a trustee to administer any Plan under Section 4042 of ERISA, or the occurrence of any event or condition which could reasonably be expected to constitute grounds under ERISA for the termination of, or the appointment of a trustee to administer, any Plan under Section 4041 Section 4042 of ERISA; (g) the incurrence by Borrower or its Subsidiaries or any of their respective ERISA Affiliates of any liability with respect to the withdrawal from any Plan or Multiemployer Plan; (h) the receipt by Borrower or its Subsidiaries or any of their respective ERISA Affiliates of any notice, concerning the imposition of Withdrawal Liability or a determination that a Multiemployer Plan is, or is expected to be, insolvent or in reorganization, within the meaning of Section 4245 or Section 4241, respectively, of ERISA; (i) the "substantial cessation of operations" by Borrower or its Subsidiaries or their ERISA Affiliates within the meaning of Section 4062(e) of ERISA with respect to a Plan; or (j) the occurrence of a nonexempt prohibited transaction (within the meaning of Section 4975 of the IRC or Section 406 of ERISA) which could reasonably be expected to result in material liability to Borrower or its Subsidiaries.

"**Event of Default**" is defined in Section 7.

"**Exchange Act**" means the Securities Exchange Act of 1934.

"**Exchange Act Documents**" is defined in Section 4.8(a).

"**Excluded Accounts**" is defined in Section 5.5.

"**Excluded Equity Interests**" means, collectively: (i) any Equity Interests in any Subsidiary with respect to which the grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien upon, and the pledge to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of, such Equity Interests, to secure the Obligations (and any guaranty thereof) are validly prohibited by Requirements of Law; (ii) any Equity Interests in any Subsidiary with respect to which the grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien upon, and the pledge to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of, such Equity Interests, to secure the Obligations (and any guaranty thereof) require the consent, approval or waiver of any Governmental Authority or other third party and such consent, approval or waiver has not been obtained by Borrower following Borrower's commercially reasonable efforts to obtain the same; (iii) any Equity Interests in any Subsidiary that is a non-Wholly-Owned Subsidiary that the grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien upon, and the pledge to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of, such Equity Interests, to secure the Obligations (and any guaranty thereof) are validly prohibited by, or would give any third party (other than Borrower or an Affiliate of Borrower) the right to terminate its obligations under, the Operating Documents or the joint venture agreement or shareholder agreement with respect to, or any other contract with such third party relating to such non-Wholly-Owned Subsidiary, including any contract evidencing Indebtedness of such non-Wholly-Owned Subsidiary (other than customary non-assignment provisions which are ineffective under Article 9 of the Code or other Requirements of Law), but only, in each case, to the extent, and for so long as such Operating Document, joint venture agreement, shareholder agreement or other contract is in effect;

(iv) any Equity Interests in any other Subsidiary with respect to which, Borrower and the Collateral Agent reasonably determine by mutual agreement that the cost (including Tax costs) of granting the Collateral Agent, for the benefit of Lenders and the other Secured Parties, a security interest in and Lien upon, and pledging to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, such Equity Interests, to secure the Obligations (and any guaranty thereof) are excessive, relative to the value to be afforded to the Secured Parties thereby.

"**Excluded Property**" has the meaning set forth in the Security Agreement.

"**Excluded Subsidiaries**" means, collectively: (i) any Subsidiary with respect to which the grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien upon, and the pledge to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of, such Subsidiary's properties and assets subject or purported to be subject from time to time to a Lien under any Collateral Document and the Equity Interests in such Subsidiary to secure the Obligations (and any guaranty thereof) are validly prohibited by Requirements of Law; (ii) any Subsidiary with respect to which the grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien upon, and the pledge to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of, such Subsidiary's properties and assets subject or purported to be subject from time to time to a Lien under any Collateral Document and the Equity Interests in such Subsidiary to secure the Obligations (and any guaranty thereof) require the consent, approval or waiver of any Governmental Authority or other third party (other than Borrower or an Affiliate of Borrower) and such consent, approval or waiver has not been obtained by Borrower or such Subsidiary following Borrower's and such Subsidiary's commercially reasonable efforts to obtain the same; (iii) any Subsidiary that is a non-Wholly-Owned Subsidiary, with respect to which, the grant to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien upon, and the pledge to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of, the properties and assets of such non-Wholly-Owned Subsidiary, to secure the Obligations (and any guaranty thereof) are validly prohibited by, or would give any third party (other than Borrower or an Affiliate of Borrower) the right to terminate its obligations under, such non-Wholly-Owned Subsidiary's Operating Documents or the joint venture agreement or shareholder agreement with respect thereto or any other contract with such third party relating to such non-Wholly-Owned Subsidiary, including any contract evidencing Indebtedness of such non-Wholly-Owned Subsidiary (other than customary non-assignment provisions which are ineffective under Article 9 of the Code or other Requirements of Law), but only, in each case, to the extent, and for so long as such Operating Document, joint venture agreement, shareholder agreement or other contract is in effect; (iv) any Subsidiary that owns properties and assets with an aggregate fair market value (reasonably determined in good faith by a Responsible Officer of Borrower) of less than $5,000,000; (v) any Subsidiary that is not a United States Person within the meaning of Section 7701(a)(30) of the IRC; and (vi) any other Subsidiary with respect to which, Borrower and the Collateral Agent reasonably determine by mutual agreement that the cost (including Tax costs) of granting the Collateral Agent, for the benefit of Lenders and the other Secured Parties, a security interest in and Lien upon, and pledging to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, such Subsidiary's properties and assets subject or purported to be subject from time to time to a Lien under any Collateral Document and the Equity Interests of such Subsidiary to secure the Obligations (and any guaranty thereof) are excessive relative to the value to be afforded to the Secured Parties thereby. For the avoidance of doubt, Global Blood Therapeutics GmbH, a Swiss limited liability company, shall be considered an Excluded Subsidiary.

"**Excluded Taxes**" means any of the following Taxes imposed on or with respect to Lender or required to be withheld or deducted from a payment to Lender, (a) Taxes imposed on or measured by net income (however denominated), franchise Taxes, and branch profits Taxes, in each case, (i) imposed by the United States or as a result of Lender being organized under the laws of, or having its principal office or its applicable lending office located in, the jurisdiction imposing such Tax (or any political subdivision thereof) or (ii) that are Other Connection Taxes, (b) U.S. federal withholding Taxes imposed on amounts payable to or for the account of Lender with respect to any Obligation pursuant to a law in effect on the date on which (i) Lender acquires such interest in any Obligation or (ii) Lender changes its lending office, except in each case to the extent that, pursuant to Section 2.6, amounts with respect to such Taxes were payable either to Lender's assignor immediately before Lender became a party hereto or to Lender immediately before it changed its lending office, (c) Taxes attributable to Lender's failure to comply with Section 2.6(d), and (d) any withholding Taxes imposed under FATCA.

"**Export and Import Laws**" means any applicable law, regulation, order or directive that applies to the import, export, re-export, transfer, disclosure or provision of goods, software, technology or technical assistance including, without limitation, restrictions or controls administered pursuant to the U.S. Export Administration Regulations, 15 C.F.R. Parts 730-774, administered by the U.S. Department of Commerce, Bureau of Industry and Security; U.S. Customs regulations; and similar import and export laws, regulations, orders and directives of other jurisdictions to the extent applicable.

"**Facility**" means, with respect to any Credit Party, any real property (including all buildings, fixtures or other improvements located thereon) now, hereafter or heretofore owned, leased, operated or used by such Credit Party or any of its Subsidiaries or any of their respective predecessors or Affiliates.

"**FATCA**" means Sections 1471 through 1474 of the IRC, as of the date of this Agreement (including, for the avoidance of doubt, any agreements between the governments of the United States and the jurisdiction in which the applicable Lender is resident implementing such provisions), or any amended or successor version that is substantively comparable and not materially more onerous to comply with, and any current or future regulations promulgated thereunder or official interpretations thereof, any agreements entered into pursuant to Section 1471(b)(1) of the IRC, any intergovernmental agreement entered into in connection with the implementation of the foregoing sections of the IRC and any fiscal or regulatory legislation, regulations, rules or practices adopted pursuant to, or official interpretations implementing such Sections of the IRC or intergovernmental agreements.

"**FCPA**" is defined in Section 4.18(a).

"**FDA**" means the United States Food and Drug Administration (and any foreign equivalent, including the European Agency for the Evaluation of Medicinal Products).

"**FDA Good Clinical Practices**" means the standards set forth in 21 C.F.R. Parts 50, 56, 312, and 314 and FDA's implementing guidance documents.

"**FDA Good Laboratory Practices**" means the standards set forth in 21 C.F.R. Part 58 and FDA's implementing guidance documents.

"**FDA Good Manufacturing Practices**" means the standards set forth in 21 C.F.R. Parts 210, 211 and 600 and FDA's implementing guidance documents.

"**FDA Laws**" means all applicable statutes (including the FDCA), rules and regulations implemented administered or enforced by the FDA (and any foreign equivalent).

"**FDCA**" is defined in Section 4.19(b).

"**Federal Reserve Board**" means the Board of Governors of the Federal Reserve System.

"**Foreign Lender**" means a Lender that is not a "United States person" as defined in Section 7701(a)(30) of the IRC.

"**GDPR**" means the General Data Protection Regulation (EU) 2016/679.

"**Governmental Approval**" means any consent, authorization, approval, order, license, franchise, permit, certificate, accreditation, registration, filing or notice, of, issued by, from or to, or other act by or in respect of, any Governmental Authority.

"**Governmental Authority**" means any nation or government, any state or other political subdivision thereof, any agency (including Regulatory Agencies), government department, authority, instrumentality, regulatory body, court, central bank or other entity exercising executive, legislative, judicial, taxing, regulatory or administrative functions of or pertaining to government, any securities exchange and any self-regulatory organization.

"**Governmental Payor Programs**" means all governmental third party payor programs in which any Credit Party or its Subsidiaries participates, including Medicare, Medicaid, TRICARE or any other federal or state health care programs.

"**Guarantor**" means any Subsidiary that is a present or future guarantor of the Obligations.

"**Hazardous Materials**" means any chemical, material or substance, exposure to which is prohibited, limited or regulated by any Governmental Authority or which may or could pose a hazard to the health and safety of the owners, occupants or any Persons in the vicinity of any Facility or to the indoor or outdoor environment.

"**Hazardous Materials Activity**" means any past, current, proposed or threatened activity, event or occurrence involving any Hazardous Materials, including the use, manufacture, possession, storage, holding, presence, existence, location, Release, threatened Release, discharge, placement, generation, transportation, processing, construction, treatment, abatement, removal, remediation, disposal, disposition or handling of any Hazardous Materials, and any corrective action or response action with respect to any of the foregoing.

"**Health Care Laws**" means, collectively: (a) applicable federal, state or local laws, rules, regulations, orders, ordinances, statutes and requirements issued under or in connection with Medicare, Medicaid or any other Government Payor Program; (b) applicable federal and state laws and regulations governing the confidentiality of health information, including HIPAA; (c) applicable federal, state and local fraud and abuse laws of any Governmental Authority, including the federal Anti-Kickback Statute (42 U.S.C. § 1320a-7(b)), the civil False Claims Act (31 U.S.C. § 3729 et seq.), Sections 1320a-7 and 1320a-7a of Title 42 of the United States Code and the regulations promulgated pursuant to such statutes; (d) the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Pub. L. No. 108-173) and the regulations promulgated thereunder; (e) the Physician Payment Sunshine Act (42 U.S.C. § 1320a-7h); (f) all applicable reporting and disclosure requirements under the Medicaid Drug Rebate Program (e.g., Monthly and Quarterly Average Manufacturer Price, Baseline Average Manufacturer Price, and Rebate Per Unit, as applicable), Medicare Part B (Quarterly Average Sales Price), Section 602 of the Veteran's Health Care Act (Public Health Service 340B Quarterly Ceiling Price), Section 603 of the Veteran's Health Care Act (Quarterly and Annual Non-Federal Average Manufacturer Price and Federal Ceiling Price), Best Price, Federal Supply Schedule Contract Prices and Tricare Retail Pharmacy Refunds, and Medicare Part D; (g) applicable health care laws, rules, codes, statutes, regulations, orders, ordinances and requirements pertaining to Medicare or Medicaid; in each case, in any manner applicable to any Credit Party or any of its Subsidiaries; (h) applicable federal, state or local laws, rules, regulations, ordinances, statutes and requirements relating to (i) the regulation of managed care, third party payors and Persons bearing the financial risk for the provision or arrangement of health care services, (ii) billings to insurance companies, health maintenance organizations and other Managed Care Plans or otherwise relating to insurance fraud and (iii) any insurance, health maintenance organization or managed care Requirements of Law; and (i) any other applicable health care laws, rules, codes, regulations, manuals, orders, ordinances, and statutes relating to the manufacture, sale and distribution of pharmaceutical products.

"**Hedging Agreement**" means any interest rate, currency, commodity or equity swap, collar, cap, floor or forward rate agreement, or other agreement or arrangement designed to protect a Person against fluctuations in interest rates, currency exchange rates or commodity or equity prices or values (including any option with respect to any of the foregoing and any combination of the foregoing agreements or arrangements), and any confirmation execution in connection with any such agreement or arrangement

"**HIPAA**" means the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) of 2009, any and all rules or regulations promulgated from time to time thereunder, and any state or federal laws with regard to the security, privacy, or notification of breaches of the confidentiality of health information which are not preempted pursuant to 45 C.F.R. Part 160, Subpart B.

"**Indebtedness**" means, with respect to any Person, without duplication: (a) all indebtedness for advanced or borrowed money of, or credit extended to, such Person; (b) all obligations issued, undertaken or assumed by such Person as the deferred purchase price of assets, properties, services or rights (other than (i) accrued expenses and trade payables entered into in the ordinary course of business consistent with past practice which are not more than one hundred and eighty (180) days past due or subject to a bona fide dispute, (ii) obligations to pay for services provided

by employees and individual independent contractors in the ordinary course of business consistent with past practice which are not more than one hundred twenty (120) days past due or subject to a bona fide dispute, (iii) liabilities associated with customer prepayments and deposits and (iv) prepaid or deferred revenue arising in the ordinary course of business consistent with past practice), including any obligation or liability to pay deferred or contingent purchase price or other similar consideration for such assets, properties, services or rights; (c) the face amount of all letters of credit issued for the account of such Person and, without duplication, all drafts drawn thereunder and all reimbursement or payment obligations with respect to letters of credit, surety bonds, performance bonds and other similar instruments issued by such Person; (d) all obligations of such Person evidenced by notes, bonds, debentures or other debt securities or similar instruments (including debt securities convertible into Equity Interests), including obligations so evidenced incurred in connection with the acquisition of properties, assets or businesses; (e) all indebtedness of such Person created or arising under any conditional sale or other title retention agreement or incurred as financing, in either case with respect to property acquired by such Person (even though the rights and remedies of the seller or bank under such agreement in the event of default are limited to repossession or sale of such property); (f) all capital lease obligations of such Person; (g) the principal balance outstanding under any synthetic lease, off-balance sheet loan or similar off balance sheet financing product by such Person; (h) all obligations of such Person, whether or not contingent, to purchase, redeem, retire, defease or otherwise acquire for value any of its own Equity Interests (or any Equity Interests of a direct or indirect parent entity thereof) prior to the date that is one hundred and eighty (180) days after the Term Loan Maturity Date, valued at, in the case of redeemable preferred Equity Interests, the greater of the voluntary liquidation preference and the involuntary liquidation preference of such Equity Interests plus accrued and unpaid dividends; (i) all indebtedness referred to in clauses (a) through (h) above of other Persons secured by (or for which the holder of such indebtedness has an existing right, contingent or otherwise, to be secured by) any Lien upon or in assets or properties (including accounts and contracts rights) owned by such Person, even though such Person has not assumed or become liable for the payment of such indebtedness of such other Persons; and (j) all Contingent Obligations of such Person.

"**Indemnified Liabilities**" means, collectively, any and all liabilities, obligations, losses, damages (including natural resource damages), penalties, claims, actions, judgments, suits, costs, reasonable and documented out-of-pocket fees, expenses and disbursements of any kind or nature whatsoever (including the reasonable and documented fees and disbursements of one counsel for Indemnified Persons plus, if required, one local legal counsel in each relevant material jurisdiction, and in the case of an actual or perceived conflict of interest, one additional counsel for such affected Indemnified Persons, in connection with any investigative, administrative or judicial proceeding or hearing commenced or threatened in writing by any Person, whether or not any such Indemnified Person shall have commenced such proceeding or hearing or be designated as a party or a potential party thereto, and any fees or expenses incurred by Indemnified Persons in enforcing the indemnity hereunder), whether direct, indirect or consequential and whether based on any federal, state or foreign laws, statutes, rules or regulations, on common law or equitable cause or on contract or otherwise, that may be imposed on, incurred by, or asserted against any such Indemnified Person, in any manner relating to or arising out of this Agreement or the other Loan Documents or the transactions contemplated hereby or thereby (including any Lender's agreement to make Credit Extensions or the use or intended use of the proceeds thereof, or any enforcement of any of the Loan Documents (including any sale of, collection from, or other realization upon any of the Collateral or the enforcement of any guaranty of the Obligations)).

"**Indemnified Person**" is defined in Section 11.2(a).

"**Indemnified Taxes**" means (a) Taxes, other than Excluded Taxes, imposed on or with respect to any payment made by or on account of any obligation of any Credit Party under any Loan Document and (b) to the extent not otherwise described in clause (a) above, Other Taxes.

"**Insolvency Proceeding**" means, with respect to any Person, any proceeding by or against such Person under the United States Bankruptcy Code, or any other bankruptcy or insolvency law, including assignments for the benefit of creditors, compositions, extensions generally with its creditors, or proceedings seeking reorganization, arrangement, or other relief.

"**Intellectual Property**" means all:

(a) Copyrights, Trademarks, and Patents;

(b) trade secrets and trade secret rights, including any rights to unpatented inventions, know-how, show-how and operating manuals;

(c) (i) all computer programs, including source code and object code versions, (ii) all data, databases and compilations of data, whether machine readable or otherwise, and (iii) all documentation, training materials and configurations related to any of the foregoing (collectively, "**Software**");

(d) all right, title and interest arising under any contract or Requirements of Law in or relating to Internet domain names;

(e) design rights;

(f) IP Ancillary Rights (including all IP Ancillary Rights related to any of the foregoing); and

(g) any similar or equivalent rights to any of the foregoing anywhere in the world.

"**Interest Date**" means the last day of each calendar quarter.

"**Interest Period**" means, with respect to the Term Loans, (a) the period commencing on (and including) the applicable borrowing date of the Term Loans and ending on (and including) the first Interest Date following such Borrowing, provided, that if such Interest Date is not a Business Day, the applicable Interest Period shall end on the first Business Day immediately following such Interest Date, and (b) thereafter, each period beginning on (and including) the first day following the end of the preceding Interest Period and ending on the earlier of (and including) (x) the next Interest Date, provided, that if any such last day is not a Business Day, the applicable Interest Period shall end on the first Business Day immediately preceding such Interest Date, (y) the next Payment Date, provided, that if any such day is not a Business Day, the applicable Interest Period shall end on the first Business Day immediately following such Payment Date and (z) the Term Loan Maturity Date. For the avoidance of doubt, if an Interest Period ends on a Payment Date, the next Interest Period shall commence on (and include) the first day following such Payment Date and shall end on (and include) the earlier of the next Interest Date, the next Payment Date or the Term Loan Maturity Date, as described above.

"**Interest Rate Determination Date**" means (a) initially, the Closing Date and (b) thereafter, the first day of each Interest Period (or, if any such day is not a Business Day, the first Business Day immediately following such day).

"**Internet Domain Name**" means all right, title and interest (and all related IP Ancillary Rights) arising under any contract or Requirements of Law in or relating to Internet domain names.

"**Inventory**" means all "inventory" as defined in the Code in effect on the date hereof with such additions to such term as may hereafter be made, and includes all merchandise, raw materials, parts, supplies, packing and shipping materials, work in process and finished products, including such inventory as is temporarily out of a Credit Party's or Subsidiary's custody or possession or in transit and including any returned goods and any documents of title representing any of the above.

"**Investment**" means (a) any beneficial ownership interest in any Person (including Equity Interests), (b) any Acquisition or (c) the making of any advance, loan, extension of credit or capital contribution in or to, any Person.

"**IP Agreements**" means, collectively, (a) those certain Intellectual Property Security Agreements entered into by and between Borrower and the Collateral Agent, each dated as of the Tranche A Closing Date, and (b) any Intellectual Property Security Agreement entered into by and between Borrower and the Collateral Agent after the Tranche A Closing Date in accordance with the Loan Documents.

"**IP Ancillary Rights**" means, with respect to any Copyright, Trademark, Patent, Software, trade secrets or trade secret rights, including any rights to unpatented inventions, know-how, show-how and operating manuals, all income, royalties, proceeds and liabilities at any time due or payable or asserted under or with respect to any of the

foregoing or otherwise with respect thereto, including all rights to sue or recover at law or in equity for any past, present or future infringement, misappropriation, dilution, violation or other impairment thereof, and, in each case, all rights to obtain any other intellectual property right ancillary to any Copyright, Trademark, Patent, Software, trade secrets or trade secret rights.

"**IRC**" means the Internal Revenue Code of 1986.

"**IRS**" is defined in Section 2.6(d)(i).

"**Knowledge**" of Borrower means the actual knowledge, after reasonable investigation, of the Responsible Officers of Borrower or such other Credit Party, as the context dictates.

"**Lender**" means each Person signatory hereto as a "Lender" and its successors and assigns.

"**Lender Expenses**" means, collectively: (i) all reasonable and documented out-of-pocket fees and expenses of the Collateral Agent and the Lenders (and their respective successors and assigns) and their respective Related Parties, taken as a whole (including the reasonable and documented out-of-pocket fees, expenses and disbursements of legal counsel therefor) (A) incurred in connection with developing, preparing, negotiating, syndicating, executing and delivering, and interpreting, investigating and administering, the Loan Documents (or any term or provision thereof), any commitment, proposal letter, letter of intent or term sheet therefor or any other document prepared in connection therewith, (B) incurred in connection with the consummation and administration of any transaction contemplated therein, (C) incurred in connection with the performance of any obligation or agreement contemplated therein or (D) incurred in connection with any modification or amendment of any term or provision of or any supplement to or the termination (in whole or in part) of, any Loan Document, (E) in connection with internal audit reviews and Collateral audits or (E) otherwise incurred with respect to the Credit Parties in connection with the Loan Documents, including any filing or recording fees and expenses; and (ii) all reasonable and documented out-of-pocket costs and expenses incurred by the Collateral Agent and each Lender (and their respective successors and assigns) and their respective Related Parties (including the reasonable and documented out-of-pocket fees, expenses and disbursements of legal counsel therefor), in connection with (A) any refinancing or restructuring of the credit arrangements provided hereunder in the nature of a "work-out", (B) the enforcement or preservation of any right or remedy under any Loan Document, any Obligation, with respect to the Collateral or any other related right or remedy, or (C) the commencement, defense, conduct of, intervention in, or the taking of any other action with respect to, any proceeding (including any Insolvency Proceeding) related to any Credit Party or any Subsidiary of any Credit Party in respect of any Loan Document or Obligation, or otherwise in connection with any Loan Document or Obligation (or the response to and preparation for any subpoena or request for document production relating thereto); provided, that, except with respect to an Insolvency Proceeding, to the extent such enforcement entails the Collateral Agent or any Lender commencing legal action of any sort against the Borrower, any fees and expenses incurred in connection therewith shall only be payable by the Borrower to the extent the Collateral Agent or any Lender is successful in such legal action.

"**Lender Transfer**" is defined in Section 11.1(b).

"**LIBOR Rate**" means, as of any Interest Rate Determination Date and for any Interest Period, the rate per annum equal to (a) the rate of interest appearing via a Bloomberg Terminal on Page US003M Index of the Bloomberg Financial Markets Information System (or any successor page) for three-month Dollar deposits or (b) if no such rate is available via a Bloomberg Terminal, the rate of interest determined by Lender to be the rate or the arithmetic mean of rates at which Dollar deposits in immediately available funds are offered to first-tier banks in the London interbank Eurodollar market, in each case under clause (a) or (b) above at approximately 11:00 a.m., London time, on such Interest Rate Determination Date for a period of three (3) months; provided, however, that, for purposes of calculating the Term Loan Rate, the LIBOR Rate shall at all times have a floor of two percent (2.00%).

"**Lien**" means a claim, mortgage, deed of trust, levy, charge, pledge, security interest or other encumbrance of any kind or assignment for security purposes, whether voluntarily incurred or arising by operation of law or otherwise against any property or assets.

"**Liquidity**" means the sum of the Credit Parties' unrestricted cash and Cash Equivalents maintained in Collateral Accounts with respect to which Control Agreements are in effect.

"**Loan Documents**" means, collectively, this Agreement, the Disclosure Letter, the Term Loan Notes, the Security Agreement, the IP Agreements, the Perfection Certificates, any Control Agreement, any other Collateral Document, any guaranties executed by a Guarantor in favor of the Collateral Agent for the benefit of Lenders and the other Secured Parties in connection with this Agreement, and any other present or future agreement between or among a Credit Party, the Collateral Agent and any Lender in connection with this Agreement, including in each case, for the avoidance of doubt, any annexes, exhibits or schedules thereto.

"**Makewhole Amount**" means the Tranche A Makewhole Amount or the Tranche B Makewhole Amount (as applicable) or any combination thereof, as the context dictates.

"**Managed Care Plans**" means all health maintenance organizations, preferred provider organizations, individual practice associations, competitive medical plans and similar arrangements.

"**Manufacturing Agreement**" means (i) any manufacturing or supply agreement entered into by any Credit Party or any of its Subsidiaries with third parties for the commercial supply in the Territory of any Product for any indication or for the commercial supply of the active pharmaceutical ingredient incorporated therein that was included in the New Drug Application for the Product (with the Manufacturing Agreements in effect as of the Effective Date being set forth in Schedule 12.1 of the Disclosure Letter), and (ii) any future manufacturing or supply agreement entered into after the Effective Date by any Credit Party or any of its Subsidiaries with third parties for the commercial supply in the Territory of any Product for any indication or for the commercial supply of the active ingredient incorporated therein.

"**Margin Stock**" means "margin stock" within the meaning of Regulations U and X of the Federal Reserve Board as now and from time to time hereafter in effect.

"**Material Adverse Change**" means any material adverse change in or effect on: (i) the business, financial condition, properties or assets (including all or any portion of the Collateral), liabilities (actual or contingent), operations, or performance of the Credit Parties, taken as a whole, since September 30, 2019; (ii) without limiting the generality of clause (i) above, the rights of the Credit Parties, taken as a whole, in or related to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of the Product in the Territory; (iii) the ability of the Credit Parties, taken as a whole, to fulfill the payment or performance obligations under this Agreement or any other Loan Document; or (iv) the binding nature or validity of, or the ability of the Collateral Agent or any Lender to enforce, the Loan Documents or any of its rights or remedies under the Loan Documents.

"**Material Contract**" means any contract or other arrangement to which any Credit Party or any of its Subsidiaries is a party (other than the Loan Documents) or by which any of its assets or properties are bound, in each case, relating to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of the Product in the Territory, for which the breach of, default or nonperformance under, cancellation or termination of or the failure to renew could reasonably be expected to result in a Material Adverse Change. For the avoidance of doubt, each Manufacturing Agreement, and each Current Company IP Agreement is a Material Contract.

"**Medicaid**" means the health care assistance program established by Title XIX of the SSA (42 U.S.C. 1396 et seq.).

"**Medicare**" means the health insurance program for the aged and disabled established by Title XVIII of the SSA (42 U.S.C. 1395 et seq.).

"**Mortgage**" means any deed of trust, leasehold deed of trust, mortgage, leasehold mortgage, deed to secure debt, leasehold deed to secure debt or other document creating a Lien on real estate or any interest in real estate.

"**Multiemployer Plan**" means a multiemployer plan within the meaning of Section 4001(a)(3) or Section 3(37) of ERISA (a) to which Borrower or its Subsidiaries or their respective ERISA Affiliates is then making or accruing an obligation to make contributions; (b) to which Borrower or its Subsidiaries or their respective ERISA Affiliates has within the preceding five (5) plan years made contributions; or (c) with respect to which Borrower or its Subsidiaries could incur material liability.

"**Obligations**" means, collectively, the Credit Parties' obligations to pay when due any and all debts, principal, interest, Lender Expenses, the Additional Consideration, the Makewhole Amount, the Prepayment Premium and any other fees, expenses, indemnities and amounts any Credit Party owes any Lender or the Collateral Agent now or later, under this Agreement or any other Loan Document, including interest accruing after Insolvency Proceedings begin (whether or not allowed), and to perform Borrower's duties under the Loan Documents.

"**OFAC**" is defined in Section 4.18(c).

"**OFAC Lists**" means, collectively, the Specially Designated Nationals and Blocked Persons List maintained by OFAC pursuant to Executive Order No. 13224, 66 Fed. Reg. 49079 (Sept. 25, 2001) or any other list of terrorists or other restricted Persons maintained pursuant to any of the rules and regulations of OFAC or pursuant to any other applicable Executive Orders.

"**Operating Documents**" means, collectively with respect to any Person such Person's formation documents as certified with the Secretary of State or other applicable Governmental Authority of such Person's jurisdiction of formation on a date that is no earlier than thirty (30) days prior to the date on which such documents are due to be delivered under this Agreement and, (a) if such Person is a corporation, its bylaws (or similar organizational regulations) in current form, (b) if such Person is a limited liability company, its limited liability company agreement (or similar agreement), and (c) if such Person is a partnership, its partnership agreement (or similar agreement), in each case, with all current amendments, restatements, supplements or modifications thereto.

"**ordinary course of business**" means, in respect of any transaction involving any Person, the ordinary course of such Person's business, undertaken by such Person in good faith and not for purposes of evading any covenant, prepayment obligation or restriction in any Loan Document.

"**Other Connection Taxes**" means, with respect to any Lender, Taxes imposed as a result of a present or former connection (including present or former connection of its agents) between such Lender and the jurisdiction imposing such Tax (other than connections arising solely from such Lender having executed, delivered, become a party to, performed its obligations under, received payments under, received or perfected a security interest under, engaged in any other transaction pursuant to or enforced any Loan Document, or sold or assigned an interest in any Term Loan or Loan Document).

"**Other Taxes**" means all present or future stamp, court or documentary, intangible, recording, filing, mortgage or property Taxes, charges or similar levies or similar Taxes that arise from any payment made hereunder, from the execution, delivery, performance, enforcement or registration of, from the receipt or perfection of a security interest under, or otherwise with respect to, any Loan Document, except any such Taxes that are Other Connection Taxes imposed with respect to an assignment.

"**Participant Register**" is defined in Section 11.1(d).

"**Patents**" means all patents and patent applications (including any improvements, continuations, continuations-in-part, divisions, provisionals or any substitute applications), any patent issued with respect to any of the foregoing patent applications, any reissue, reexamination, renewal or patent term extension or adjustment (including any supplementary protection certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign and international counterparts of any of the foregoing. For the avoidance of doubt, patents and patent applications under this definition include all those filed with the U.S. Patent and Trademark Office or which could be nationalized in the United States.

"**Patriot Act**" is defined in Section 3.1(i).

"**Payment/Advance Request**" means a Payment/Advance Request in substantially the form attached hereto as Exhibit A.

"**Payment Date**" means, with respect to the Tranche A Loan and the Tranche B Loan, as applicable, (a) the Interest Date immediately following each of the date that is (1) the 39th-month anniversary of the Tranche A Closing Date, (2) the 42nd-month anniversary of the Tranche A Closing Date, (3) the 45th-month anniversary of the Tranche A Closing Date, (4) the 48th-month anniversary of the Tranche A Closing Date, (5) the 51st-month anniversary of the Tranche A Closing Date, (6) the 54th-month anniversary of the Tranche A Closing Date, (7) the 57th-month anniversary of the Tranche A Closing Date, (8) the 60th-month anniversary of the Tranche A Closing Date, (9) the 63rd-month anniversary of the Tranche A Closing Date, (10) the 66th-month anniversary of the Tranche A Closing Date, and (11) the 69th-month anniversary of the Tranche A Closing Date, and (b) the Term Loan Maturity Date, as the context dictates.

"**Perfection Certificate**" is defined in Section 4.6.

"**Permitted Acquisition**" means any Acquisition, so long as:

(a) no Default or Event of Default shall have occurred and be continuing as of, or could reasonably be expected to result from, the consummation of such Acquisition;

(b) the properties or assets being acquired or licensed, or the Person whose Equity Interests are being acquired, are useful in or engaged in, as applicable, (i) the same or a related line of business as that then-conducted by Borrower or its Subsidiaries, or (ii) a line of business that is ancillary to and in furtherance of a line of business as that then-conducted by Borrower or its Subsidiaries;

(c) in the case of an Asset Acquisition, the subject assets are being acquired or licensed by a Credit Party, and such Credit Party shall have executed and delivered or authorized, as applicable, any and all security agreements, financing statements and any other documentation reasonably requested by the Collateral Agent, in order to include the newly acquired or licensed assets within the Collateral, as applicable, to the extent required by Section 5.12;

(d) in the case of a Stock Acquisition, the subject Equity Interests are being acquired in such Acquisition directly by a Credit Party, and such Credit Party shall have complied with its obligations under Section 5.13; and

(e) any Indebtedness or Liens assumed in connection with such Acquisition are otherwise permitted under Section 6.4 or 6.5, respectively.

"**Permitted Distributions**" means, in each case subject to Section 6.8 if applicable:

(a) dividends, distributions or other payments by any Wholly-Owned Subsidiary on its Equity Interests to, or the redemption, retirement or purchase by any Wholly-Owned Subsidiary of its Equity Interests from, Borrower or any other Wholly-Owned Subsidiary;

(b) dividends, distributions or other payments by any non-Wholly-Owned Subsidiary on its Equity Interests to, or the redemption, retirement or purchase by any non-Wholly-Owned Subsidiary of its Equity Interests from, Borrower or any other Subsidiary or each other owner of such non-Wholly-Owned Subsidiary's Equity Interests based on their relative ownership interests of the relevant class of such Equity Interests;

(c) redemptions by Borrower in whole or in part any of its Equity Interests for another class of its Equity Interests or rights to acquire its Equity Interests or with proceeds from substantially concurrent equity contributions or issuances of new Equity Interests;

(d) any such payments arising from a Permitted Acquisition or other Permitted Investment by Borrower or any of its Subsidiaries;

(e) the payment of dividends by Borrower solely in non-cash pay and non-redeemable capital stock (including, for the avoidance of doubt, dividends and distributions payable solely in Equity Interests);

(f) cash payments in lieu of the issuance of fractional shares arising out of stock dividends, splits or combinations or in connection with the exercise of warrants, options or other securities convertible into or exchangeable for Equity Interests;

(g) in connection with any Acquisition or other Investment by Borrower or any of its Subsidiaries, (i) the receipt or acceptance of the return to Borrower or any of its Subsidiaries of Equity Interests of Borrower constituting a portion of the purchase price consideration in settlement of indemnification claims, or as a result of a purchase price adjustment (including earn-outs or similar obligations) and (ii) payments or distributions to equity holders pursuant to appraisal rights required under Requirements of Law;

(h) the distribution of rights pursuant to any shareholder rights plan or the redemption of such rights for nominal consideration in accordance with the terms of any shareholder rights plan;

(i) dividends, distributions or payments on its Equity Interests by any Subsidiary to any Credit Party;

(j) dividends, distributions or payments on its Equity Interests by any Subsidiary that is not a Credit Party to any other Subsidiary that is not a Credit Party;

(k) purchases of Equity Interests of Borrower or its Subsidiaries in connection with the exercise of stock options by way of cashless exercise, or in connection with the satisfaction of withholding tax obligations;

(l) issuance to directors, officers, employees or contractors of Borrower of common stock of Borrower upon the vesting of restricted stock, restricted stock units, or other rights to acquire common stock of Borrower pursuant to plans or agreements approved by Borrower's Board of Directors or stockholders;

(m) the repurchase, retirement or other acquisition or retirement for value of Equity Interests of Borrower or any of its Subsidiaries held by any future, present or former employee, consultant, officer or director (or spouse, ex-spouse or estate of any of the foregoing or trust for the benefit of any of the foregoing or any lineal descendants thereof) of Borrower or any of its Subsidiaries pursuant to any management equity plan or stock option plan or any other management or employee benefit plan or agreement, or any stock subscription or shareholder agreement or employment agreement; provided, however, that the aggregate payments made under this clause (m) do not exceed in any calendar year the sum of (i) $3,000,000 plus (ii) the amount of any payments received in such calendar year under key-man life insurance policies; and

(n) dividends or distributions on its Equity Interests by Borrower payable solely in additional shares of its common stock within sixty (60) days after the date of declaration thereof.

"**Permitted Indebtedness**" means:

(a) Indebtedness of the Credit Parties to Secured Parties under this Agreement and the other Loan Documents;

(b) Indebtedness existing on the Effective Date and shown on Schedule 12.2 of the Disclosure Letter;

(c) RESERVED;

(d) Indebtedness not to exceed $5,000,000 in the aggregate at any time outstanding, consisting of (i) Indebtedness incurred to finance the purchase, construction, repair, or improvement of fixed assets and (ii) capital lease obligations;

(e) unsecured Indebtedness in connection with corporate credit cards, purchasing cards or bank card products;

(f) guarantees of Permitted Indebtedness;

(g) Indebtedness assumed in connection with any Permitted Acquisition or Permitted Investment, so long as such Indebtedness (i) was not incurred in connection with, or in anticipation of, such Acquisition or Investment and (ii) is at all times Subordinated Debt;

(h) Indebtedness of Borrower or any of its Subsidiaries with respect to letters of credit outstanding and secured solely by cash or Cash Equivalents entered into in the ordinary course of business;

(i) Indebtedness owed (i) by a Credit Party to another Credit Party, (ii) by a Subsidiary of Borrower that is not a Credit Party to another Subsidiary of Borrower that is not a Credit Party, (iii) by a Credit Party to a Subsidiary of Borrower that is not a Credit Party or (iv) by a Subsidiary of Borrower that is not a Credit Party to a Credit Party, not to exceed $10,000,000 in the aggregate at any time outstanding;

(j) Indebtedness consisting of Contingent Obligations set forth in clause (a) of the definition of "Contingent Obligation" (i) of a Credit Party of Permitted Indebtedness (or obligations that are not Indebtedness) of another Credit Party, (ii) of a Subsidiary of Borrower which is not a Credit Party of Permitted Indebtedness (or obligations that are not Indebtedness) of another Subsidiary of Borrower which is not a Credit Party, (iii) of a Subsidiary of Borrower which is not a Credit Party of Permitted Indebtedness (or obligations that are not Indebtedness) of a Credit Party, (iv) of a Credit Party of lease obligations of a Subsidiary of Borrower which is not a Credit Party, or (v) of a Credit Party of Permitted Indebtedness (or obligations that are not Indebtedness) of a Subsidiary of Borrower which is not a Credit Party not to exceed $10,000,000 in the aggregate at any time outstanding;

(k) Indebtedness consisting of Contingent Obligations (i) set forth in clause (b) of the definition of "Contingent Obligation", and (ii) set forth in clause (c) of the definition of "Contingent Obligation" in connection with any Permitted Acquisition, not to exceed $10,000,000 in the aggregate at any time outstanding;

(l) Indebtedness of any Person that becomes a Subsidiary (or of any Person not previously a Subsidiary that is merged or consolidated with or into a Subsidiary in a transaction permitted hereunder) of Borrower after the Effective Date, or Indebtedness of any Person that is assumed after the Effective Date by any Subsidiary in connection with an acquisition of assets by such Subsidiary; provided that such Indebtedness is at all times Subordinated Debt;

(m) (i) Indebtedness with respect to workers' compensation claims, payment obligations in connection with health, disability or other types of social security benefits, unemployment or other insurance obligations, reclamation and statutory obligations or (ii) Indebtedness related to employee benefit plans, including annual employee bonuses, accrued wage increases and 401(k) plan matching obligations; in each case, incurred in the ordinary course of business consistent with past practice;

(n) Indebtedness in respect of performance bonds, bid bonds, appeal bonds, surety bonds and completion guarantees and similar obligations arising in the ordinary course of business consistent with past practice;

(o) Indebtedness in respect of netting services, overdraft protection and other cash management services, in each case in the ordinary course of business consistent with past practice;

(p) Indebtedness consisting of the financing of insurance premiums in the ordinary course of business consistent with past practice;

(q) Indebtedness consisting of guarantees resulting from endorsement of negotiable instruments for collection by any Credit Party in the ordinary course of business consistent with past practice;

(r) unsecured Indebtedness incurred in connection with any items of Permitted Distributions in clause (m) of the definition of "Permitted Distributions";

(s) Subordinated Debt, not to exceed $10,000,000 in the aggregate at any time outstanding, or such greater amount, as otherwise agreed to in writing by the Collateral Agent; and

(t) subject to the proviso immediately below, extensions, refinancings, modifications, amendments, restatements and, in the case of any items of Permitted Indebtedness in clause (b) of the definition of "Permitted Indebtedness" or Permitted Indebtedness constituting notes governed by an indenture, exchanges, of any items of Permitted Indebtedness in clauses (a) through (s) above, provided, that in the case of clauses (b) and (g) above, the principal amount thereof is not increased (other than by any reasonable amount of premium (if any), interest (including post-petition interest), fees, expenses, charges or additional or contingent interest reasonably incurred in connection with the same and the terms thereof).

Notwithstanding the foregoing, "Permitted Indebtedness" shall not include any Hedging Agreements.

"**Permitted Investments**" means:

(a) Investments (including Investments in Subsidiaries) existing on the Effective Date and shown on Schedule 12.3 of the Disclosure Letter, and any extensions, renewals or reinvestments thereof;

(b) Investments consisting of cash and Cash Equivalents;

(c) Investments consisting of the endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of business consistent with past practice;

(d) subject to Section 5.5, Investments consisting of deposit accounts or securities accounts;

(e) Investments in connection with Permitted Transfers;

(f) Investments consisting of (i) travel advances and employee relocation loans and other employee advances in the ordinary course of business consistent with past practice, and (ii) loans to employees, officers or directors relating to the purchase of equity securities of Borrower pursuant to employee stock purchase plans or agreements approved by Borrower's Board of Directors;

(g) Investments (including debt obligations) received in connection with the bankruptcy or reorganization of customers or suppliers and in settlement of delinquent obligations of, and other disputes with, customers or suppliers arising in the ordinary course of business consistent with past practice;

(h) Investments consisting of notes receivable of, or prepaid royalties and other credit extensions, to customers and suppliers who are not Affiliates, in the ordinary course of business consistent with past practice; provided that this clause (h) shall not apply to Investments of any Credit Party in any of its Subsidiaries;

(i) joint ventures or strategic alliances consisting of the non-exclusive licensing of technology, the development of technology or the providing of technical support;

(j) Investments (i) required in connection with a Permitted Acquisition (including the formation of any Subsidiary for the purpose of effectuating such Permitted Acquisition, the capitalization of such Subsidiary whether by capital contribution or intercompany loans, in each case, to the extent otherwise permitted by the terms of this Agreement, related Investments in Subsidiaries necessary to consummate such Permitted Acquisition, and the receipt of any non-cash consideration in a Permitted Acquisition), and (ii) consisting of earnest money deposits required in connection with a Permitted Acquisition or other acquisition of properties or assets not otherwise prohibited hereunder;

(k) Investments constituting the formation of any Subsidiary for the purpose of consummating a merger or acquisition transaction permitted by Section 6.3(a)(i) through (iv) hereof, which such transaction is otherwise a Permitted Investment;

(l) Investments of any Person that (i) becomes a Subsidiary of Borrower (or of any Person not previously a Subsidiary of Borrower that is merged or consolidated with or into a Subsidiary of Borrower in a transaction permitted hereunder) after the Effective Date, or (ii) are assumed after the Effective Date by any Subsidiary

of Borrower in connection with an acquisition of assets from such Person by such Subsidiary, in either case, in a Permitted Acquisition; provided, that in each case, any such Investment (x) exists at the time such Person becomes a Subsidiary of Borrower (or is merged or consolidated with or into a Subsidiary of Borrower) or such assets are acquired, (y) was not made in contemplation of or in connection with such Person becoming a Subsidiary of Borrower (or merging or consolidating with or into a Subsidiary of Borrower) or such acquisition of assets, and (z) could not reasonably be expected to result in a Default or an Event of Default;

(m) Investments arising as a result of the licensing of Intellectual Property in the ordinary course of business consistent with past practice and not prohibited hereunder;

(n) Investments by (i) any Credit Party in any other Credit Party, (ii) any Subsidiary of Borrower which is not a Credit Party in another Subsidiary of Borrower which is not a Credit Party, (iii) any Subsidiary of Borrower which is not a Credit Party in any Credit Party and (iv) any Credit Party in a Subsidiary of Borrower which is not a Credit Party not to exceed $10,000,000 in the aggregate at any time; and

(o) Repurchases of capital stock of Borrower or any of its Subsidiaries deemed to occur upon the exercise of options, warrants or other rights to acquire capital stock of Borrower or such Subsidiary solely to the extent that shares of such capital stock represent a portion of the exercise price of such options, warrants or such rights;

(p) Investments permitted under Section 1 – Approved Investments, in the Borrower's Investment Policy, dated as of November 6, 2019.[1]

provided, however, that, none of the foregoing Investments shall be a "Permitted Investment" if any Indebtedness or Liens assumed in connection with such Investment are not otherwise permitted under Section 6.4 or 6.5, respectively.

Notwithstanding the foregoing, "Permitted Investments" shall not include any Hedging Agreements.

"**Permitted Liens**" means:

(a) Liens in favor and for the benefit of any Lender and the other Secured Parties securing the Obligations pursuant to any Loan Document;

(b) Liens existing on the Effective Date and set forth on Schedule 12.4 of the Disclosure Letter;

(c) Liens for Taxes, assessments or governmental charges (i) which are not yet delinquent or (ii) which are being contested in good faith and by appropriate proceedings promptly instituted and diligently conducted; provided that adequate reserves therefor have been set aside on the books of the applicable Person and maintained in conformity with Applicable Accounting Standards, if required; provided, further, that in the case of a Tax, assessment or charge that has or may become a Lien against any Collateral, such contest proceedings conclusively operate to stay the sale or forfeiture of any portion of any Collateral to satisfy such Tax, assessment or charge;

(d) pledges or deposits made in the ordinary course of business (other than Liens imposed by ERISA) in connection with workers' compensation, payroll taxes, unemployment insurance, old-age pensions, or other similar social security legislation, (ii) pledges or deposits made in the ordinary course of business consistent with past practice securing liability for reimbursement or indemnification obligations of (including obligations in respect of letters of credit or bank guarantees for the benefit of) insurance carriers providing property, casualty or liability insurance to Borrower or any of its Subsidiaries, (iii) subject to Section 6.2(b), statutory or common law Liens of landlords, and (iv) pledges or deposits to secure performance of tenders, bids, leases, statutory or regulatory obligations, surety and appeal bonds, government contracts, performance and return-of-money bonds and other obligations of like nature, in each case other than for borrowed money and entered into in the ordinary course of business consistent with past practice;

1 OK assuming agreement on proposed changes in this mark-up.

(e) Liens arising from attachments or judgments, orders, or decrees in circumstances not constituting an Event of Default under either Section 7.4 or 7.7;

(f) Liens (including the right of set-off) in favor of banks or other financial institutions incurred on deposits made in accounts held at such institutions in the ordinary course of business; provided that such Liens (i) are not given in connection with the incurrence of any Indebtedness, (ii) relate solely to obligations for administrative and other banking fees and expenses incurred in the ordinary course of business in connection with the establishment or maintenance of such accounts and (iii) are within the general parameters customary in the banking industry;

(g) Liens that are contractual rights of set-off (i) relating to pooled deposit or sweep accounts of Borrower or any of its Subsidiaries to permit satisfaction of overdraft or similar obligations incurred in the ordinary course of business consistent with past practice or (ii) relating to purchase orders and other agreements entered into with customers of Borrower or any of its Subsidiaries in the ordinary course of business consistent with past practice;

(h) Liens solely on any cash earnest money deposits made by Borrower or any of its Subsidiaries in connection with any Permitted Acquisition, Permitted Investment or other acquisition of assets or properties not otherwise prohibited under this Agreement;

(i) Liens existing on assets or properties at the time of its acquisition or existing on the assets or properties of any Person at the time such Person becomes a Subsidiary of Borrower, in each case after the Effective Date; provided that (i) neither such Lien was created nor the Indebtedness secured thereby was incurred in contemplation of such acquisition or such Person becoming a Subsidiary of Borrower, (ii) such Lien does not extend to or cover any other assets or properties (other than the proceeds or products thereof and other than after-acquired assets or properties subject to a Lien securing Indebtedness and other obligations incurred prior to such time and which Indebtedness and other obligations are permitted hereunder that requires, pursuant to its terms and conditions in effect at such time, a pledge of after-acquired assets or properties, it being understood that such requirement shall not be permitted to apply to any assets or properties to which such requirement would not have applied but for such acquisition), (iii) the Indebtedness and other obligations secured thereby is permitted under Section 6.4 hereof and (iv) such Liens are of the type otherwise permitted under Section 6.5 hereof;

(j) Liens securing Indebtedness permitted under clause (d)(i) of the definition of "Permitted Indebtedness" (including any extensions, refinancings, modifications, amendments or restatements of such Indebtedness permitted under clause (r) of the definition of "Permitted Indebtedness"); provided, that such Lien does not extend to or cover any assets or properties other than those described in clause (d)(i) of the definition of "Permitted Indebtedness";

(k) servitudes, easements, rights-of-way, restrictions and other similar encumbrances on real property imposed by Requirements of Law and encumbrances consisting of zoning or building restrictions, easements, licenses, restrictions on the use of property or minor defects or other irregularities in title which, in the aggregate, are not material, and which do not in any case materially detract from the value of the property subject thereto or interfere with the ordinary conduct of the business of any Credit Party or any Subsidiary of any Credit Party;

(l) to the extent constituting a Lien, escrow arrangements securing indemnification obligations associated with any Permitted Acquisition or Permitted Investment;

(m) licenses, sublicenses, leases or subleases of personal property (other than relating to Intellectual Property) granted to third parties in the ordinary course of business consistent with past practice, in each case which do not interfere in any material respect with the operations of the business of any Credit Party or any of its Subsidiaries and do not prohibit granting the Collateral Agent a security interest therein for the benefit of the Lenders and other Secured Parties;

(n) Liens on cash or other current assets pledged to secure (i) Indebtedness in respect of corporate credit cards, purchasing cards or bank card products, or (ii) Indebtedness in the form of letters of credit or bank guarantees;

(o) Liens on any properties or assets of Borrower or any of its Subsidiaries which do not constitute Collateral under the Loan Documents, other than (i) any Company IP that does not constitute Collateral under the Loan Documents but is related to any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of the Product in the Territory and (ii) Equity Interests of any Subsidiary;

(p) Liens on any properties or assets of Borrower or any of its Subsidiaries imposed by law or regulation which were incurred in the ordinary course of business, including landlords', carriers', warehousemen's, mechanics', materialmen's, contractors', suppliers of materials', architects' and repairmen's Liens, and other similar Liens arising in the ordinary course of business consistent with past practice; provided that such Liens (i) do not materially detract from the value of such properties or assets subject thereto or materially impair the use of such properties or assets subject thereto in the operations of the business of Borrower or such Subsidiary or (ii) are being contested in good faith by appropriate proceedings, which conclusively operate to stay the sale or forfeiture of any portion of such properties or assets subject thereto and for which adequate reserves have been set aside on the books of the applicable Person and maintained in conformity with Applicable Accounting Standards, if required; and

(q) subject to the provisos immediately below, the modification, replacement, extension or renewal of the Liens described in clauses (a) through (p) above; provided, however, that any such modification, replacement, extension or renewal must (i) be limited to the assets or properties encumbered by the existing Lien (and any additions, accessions, parts, improvements and attachments thereto and the proceeds thereof) and (ii) not increase the principal amount of any Indebtedness secured by the existing Lien (other than by any reasonable premium or other reasonable amount paid and fees and expenses reasonably incurred in connection therewith); provided, further, that to the extent any of the Liens described in clauses (a) through (p) above secure Indebtedness of a Credit Party, such Liens, and any such modification, replacement, extension or renewal thereof, shall constitute Permitted Liens if and only to the extent that such Indebtedness is permitted under Section 6.4 hereof.

"**Permitted Negative Pledges**" means:

(a) prohibitions or limitations with regard to specific properties or assets encumbered by Permitted Liens, if and only to the extent each such prohibition or limitation applies only to such properties or assets;

(b) prohibitions or limitations set forth in any lease, license or other similar agreement entered into in the ordinary course of business;

(c) prohibitions or limitations relating to Permitted Indebtedness, in the case of each such agreement if and only to the extent such prohibitions or limitations, taken as a whole, are not materially more restrictive than the prohibitions and limitations set forth in this Agreement and the other Loan Documents, taken as a whole (as reasonably determined by a Responsible Officer of Borrower in good faith);

(d) customary provisions restricting assignments, subletting, sublicensing or other transfer of properties or assets subject thereto set forth in leases, subleases, licenses and other similar agreements that are not otherwise prohibited under this Agreement or any other Loan Document, if and only to the extent each such restriction applies only to the properties or assets subject to such leases, subleases, licenses or agreements, and customary provisions restricting assignment, pledges or transfer of any agreement entered into in the ordinary course of business consistent with past practice;

(e) prohibitions or limitations imposed by Requirements of Law;

(f) prohibitions or limitations that exist as of the Effective Date under Indebtedness existing on the Effective Date;

(g) customary prohibitions or limitations arising in connection with any Permitted Transfer or contained in any agreement relating to any Permitted Transfer pending the consummation of such Permitted Transfer;

(h) customary provisions in shareholders' agreements, joint venture agreements, organizational documents or similar binding agreements relating to, or any agreement evidencing Indebtedness of, any joint venture entity or non-Wholly-Owned Subsidiary and applicable solely to such joint venture entity or non-Wholly-Owned Subsidiary and the Equity Interests issued thereby;

(i) customary net worth provisions set forth in real property leases entered into by Subsidiaries of Borrower, so long as such net worth provisions could not reasonably be expected to impair the ability of Borrower or its Subsidiaries to meet their ongoing obligations (as reasonably determined by a Responsible Officer of Borrower in good faith);

(j) customary net worth provisions set forth in customer agreements entered into in the ordinary course of business consistent with past practice that are not otherwise prohibited under this Agreement or any other Loan Document, so long as such net worth provisions could not reasonably be expected to impair the ability of Borrower or its Subsidiaries to meet their ongoing obligations (as reasonably determined by a Responsible Officer of Borrower in good faith);

(k) restrictions on cash or other deposits (including escrowed funds) imposed by agreements entered into in the ordinary course of business consistent with past practice that are not otherwise prohibited under this Agreement or any other Loan Document;

(l) prohibitions or limitations set forth in any agreement in effect at the time any Person becomes a Subsidiary (but not any amendment, modification, restatement, renewal, extension, supplement or replacement expanding the scope of any such restriction or condition); provided that such agreement was not entered into in contemplation of such Person becoming a Subsidiary and each such prohibition or limitation does not apply to Borrower or any other Subsidiary (other than such Person and any other Person that is a Subsidiary of such first Person at the time such first Person becomes a Subsidiary);

(m) prohibitions or limitations imposed by any Loan Document;

(n) customary provisions set forth in joint venture agreements or agreements governing minority investments that are not otherwise prohibited by this Agreement or any other Loan Document, if and only to the extent each such prohibition or limitation applies only to the joint venture entity or minority investment that is the subject of such agreement;

(o) limitations imposed with respect to any license acquired in a Permitted Acquisition;

(p) customary provisions restricting assignments or other transfer of properties or assets subject thereto set forth in any agreement entered into in the ordinary course of business consistent with past practice, if and only to the extent each such restriction applies only to the properties or assets subject to such agreement;

(q) prohibitions or limitations imposed by any agreement evidencing any Permitted Indebtedness of the type described in any of clause (d) of the definition of "Permitted Indebtedness"; and

(r) prohibitions or limitations imposed by any amendments, modifications, restatements, renewals, extensions, supplements or replacements of any of the agreements referred to in clauses (a) through (p) above, except to the extent that any such amendment, modification, restatement, renewal, extension, supplement or replacement expands the scope of any such prohibition or limitation.

"**Permitted Subsidiary Distribution Restrictions**" means, in each case notwithstanding Section 6.8:

(a) prohibitions or limitations with regard to specific properties or assets encumbered by Permitted Liens, if and only to the extent each such prohibition or limitation applies only to such properties or assets;

(b) prohibitions or limitations set forth in any lease, license or other similar agreement entered into in the ordinary course of business;

(c) prohibitions or limitations relating to Permitted Indebtedness, in the case of each such agreement if and only to the extent such prohibitions or limitations, taken as a whole, are not materially more restrictive than the prohibitions and limitations set forth in this Agreement and the other Loan Documents, taken as a whole (as reasonably determined by a Responsible Officer of Borrower in good faith);

(d) customary provisions restricting assignments, subletting, sublicensing or other transfer of properties or assets subject thereto set forth in leases, subleases, licenses and other similar agreements that are not otherwise prohibited under this Agreement or any other Loan Document, if and only to the extent each such restriction applies only to the properties or assets subject to such leases, subleases, licenses or agreements, and customary provisions restricting assignment, pledges or transfer of any agreement entered into in the ordinary course of business consistent with past practice;

(e) prohibitions or limitations on the transfer or assignment of any properties, assets or Equity Interests set forth in any agreement entered into in the ordinary course of business consistent with past practice that is not otherwise prohibited under this Agreement or any other Loan Document, if and only to the extent each such prohibition or limitation applies only to such properties, assets or Equity Interests;

(f) prohibitions or limitations imposed by Requirements of Law;

(g) prohibitions or limitations that exist as of the Effective Date under Indebtedness existing on the Effective Date;

(h) customary prohibitions or limitations arising in connection with any Permitted Transfer or contained in any agreement relating to any Permitted Transfer pending the consummation of such Permitted Transfer;

(i) customary provisions in shareholders' agreements, joint venture agreements, organizational documents or similar binding agreements relating to, or any agreement evidencing Indebtedness of, any joint venture entity or non-Wholly-Owned Subsidiary and applicable solely to such joint venture entity or non-Wholly-Owned Subsidiary and the Equity Interests issued thereby;

(j) customary net worth provisions set forth in real property leases entered into by Subsidiaries of Borrower, so long as such net worth provisions could not reasonably be expected to impair the ability of Borrower or its Subsidiaries to meet their ongoing obligations (as reasonably determined by a Responsible Officer of Borrower in good faith);

(k) customary net worth provisions set forth in customer agreements entered into in the ordinary course of business consistent with past practice that are not otherwise prohibited under this Agreement or any other Loan Document, so long as such net worth provisions could not reasonably be expected to impair the ability of Borrower or its Subsidiaries to meet their ongoing obligations (as reasonably determined by a Responsible Officer of Borrower in good faith);

(l) restrictions on cash or other deposits (including escrowed funds) imposed by agreements entered into in the ordinary course of business consistent with past practice that are not otherwise prohibited under this Agreement or any other Loan Document;

(m) prohibitions or limitations set forth in any agreement in effect at the time any Person becomes a Subsidiary (but not any amendment, modification, restatement, renewal, extension, supplement or replacement expanding the scope of any such restriction or condition); provided that such agreement was not entered into in contemplation of such Person becoming a Subsidiary and each such prohibition or limitation does not apply to Borrower or any other Subsidiary (other than such Person and any other Person that is a Subsidiary of such first Person at the time such first Person becomes a Subsidiary);

(n) prohibitions or limitations imposed by any Loan Document;

(o) customary provisions set forth in joint venture agreements or agreements governing minority investments that are not otherwise prohibited by this Agreement or any other Loan Document, if and only to the extent each such prohibition or limitation applies only to the joint venture entity or minority investment that is the subject of such agreement;

(p) customary provisions restricting assignments or other transfer of properties or assets subject thereto set forth in any agreement entered into in the ordinary course of business consistent with past practice, if and only to the extent each such restriction applies only to the properties or assets subject to such agreement;

(q) prohibitions or limitations imposed by any agreement evidencing any Permitted Indebtedness of the type described in any of clause (d) of the definition of "Permitted Indebtedness"; and

(r) prohibitions or limitations imposed by any amendments, modifications, restatements, renewals, extensions, supplements or replacements of any of the agreements referred to in clauses (a) through (p) above, except to the extent that any such amendment, modification, restatement, renewal, extension, supplement or replacement expands the scope of any such prohibition or limitation.

"**Permitted Transfers**" means:

(a) Transfers of any properties or assets which do not constitute Collateral under the Loan Documents, other than any Company IP that does not constitute Collateral under the Loan Documents but is related to any research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory;

(b) Transfers of Inventory in the ordinary course of business consistent with past practice;

(c) Transfers of surplus, damaged, worn out or obsolete equipment that is, in the reasonable judgment of Borrower exercised in good faith, no longer economically practicable to maintain or useful in the ordinary course of business consistent with past practice, and Transfers of other properties or assets in lieu of any pending or threatened institution of any proceedings for the condemnation or seizure of such properties or assets or for the exercise of any right of eminent domain;

(d) Transfers made in connection with Permitted Liens;

(e) Transfers of cash and Cash Equivalents in the ordinary course of business for equivalent value and in a manner that is not prohibited by the terms of this Agreement or the other Loan Documents;

(f) Transfers (i) between or among Credit Parties, provided that, with respect to any properties or assets constituting Collateral under the Loan Documents, any and all steps as may be required to be taken in order to create and maintain a first priority security interest in and Lien upon such properties and assets in favor of the Collateral Agent for the benefit of Lenders and the other Secured Parties are taken contemporaneously with the completion of any such Transfer, and (ii) between or among non-Credit Parties;

(g) the sale or issuance of Equity Interests of any Subsidiary of Borrower to any Credit Party or Subsidiary, provided, that any such sale or issuance by a Credit Party shall be to another Credit Party;

(h) the discount without recourse or sale or other disposition of unpaid and overdue accounts receivable arising in the ordinary course of business consistent with past practice in connection with the compromise, collection or settlement thereof and not part of a financing transaction;

(i) any abandonment, cancellation, non-renewal or discontinuance of use or maintenance of Company IP that Borrower reasonably determines in good faith (i) is no longer economically practicable to maintain or useful in the ordinary course of business consistent with past practice and that (ii) could not reasonably be expected to be adverse to the rights, remedies and benefits available to, or conferred upon, the Collateral Agent or any Lender under any Loan Document in any material respect;

(j) Transfers by Borrower or any of its Subsidiaries pursuant to: (i) a non-exclusive license of (or grant of a covenant not to sue with respect to) Intellectual Property or a non-exclusive grant of development, manufacturing, production, commercialization, marketing, co-promotion, distribution, sale or similar commercial rights to third parties in the ordinary course of business consistent with general market practice, in each case except to the extent relating in any way to any Product with respect to geography within the Territory; (ii) an exclusive license of (or grant of a covenant not to sue with respect to) Intellectual Property or an exclusive grant of development, manufacturing, production, commercialization, marketing, co-promotion, distribution, sale or similar commercial rights, to third parties, in each case except to the extent relating in any way to any Product with respect to geography within the Territory; (iii) a non-exclusive license of (or grant of a covenant not to sue with respect to) technology or Intellectual Property to third parties for developing technology or providing technical support in the ordinary course of business consistent with general market practice, in each case except to the extent relating in any way to any Product with respect to geography within the Territory; and (iv) a non-exclusive or an exclusive manufacturing license to third parties in the ordinary course of business consistent with general market practice, in each case except to the extent relating in any way to any Product with respect to geography within the Territory; provided, that an exclusive or non-exclusive license out of Intellectual Property relating to any Product with respect to geography outside of the Territory that is not otherwise prohibited under this Agreement or any other Loan Document shall constitute a Permitted Transfer; provided, further, that a Transfer of Intellectual Property unrelated in any way to any Product with respect to geography within or outside the Territory that is not otherwise prohibited under this Agreement or any other Loan Document shall constitute a Permitted Transfer; and

(k) intercompany licenses or grants of rights of distribution, co-promotion or similar commercial rights between or among the Credit Parties, or (ii) between or among the Credit Parties and Subsidiaries that are not Credit Parties entered into prior to the Effective Date, and renewals, replacements and extensions thereof (including additional licenses or grants in relation to new territories) on comparable terms in the ordinary course of business consistent with past practice.

"**Person**" means any individual, sole proprietorship, partnership, limited liability company, joint venture, company, trust, unincorporated organization, association, corporation, institution, public benefit corporation, firm, joint stock company, estate, entity or government agency.

"**Pharmakon Lender**" means BioPharma Credit PLC, BioPharma Credit Investments V (Master) LP and any of their respective Controlled Investment Affiliates.

"**Plan**" means any employee pension benefit plan (other than a Multiemployer Plan) subject to the provisions of Title IV of ERISA or Section 412 of the IRC or Section 302 of ERISA which is maintained or contributed to by Borrower or its Subsidiaries or their respective ERISA Affiliates or with respect to which Borrower or its Subsidiaries have any liability (including under Section 4069 of ERISA).

"**Prepayment Premium**" means the Tranche A Prepayment Premium or the Tranche B Prepayment Premium (as applicable) or both of the Tranche A Prepayment Premium and the Tranche B Prepayment Premium, as the context dictates.

"**Private Third Party Payor Programs**" means all U.S. third party payor programs in which any Credit Party or its Subsidiaries participates, including Managed Care Plans, or any other private insurance programs, but excluding all Governmental Payor Programs.

"**Product**" means, collectively, (i) Oxbryta (voxelotor, previously called GBT440), (ii) any successor to Oxbryta, (iii) any other product marketed by any Credit Party for use in the treatment of sickle cell disease by inhibiting polymerization of hemoglobin S (HbS) as one or more of its primary mechanisms of action, and (iv) any Competing Product pursuant to Section 5.2(d).[2]

[2] Note to Goodwin – deletion of language providing that the Product is not a controlled substance is because it is already covered in section 4.19(c).

"**Register**" is defined in Section 2.8(a).

"**Registered Organization**" means any "registered organization" as defined in the Code with such additions to such term as may hereafter be made.

"**Regulatory Agency**" means a U.S. Governmental Authority with responsibility for the approval of the marketing and sale of pharmaceuticals or other regulation of pharmaceuticals, including the FDA.

"**Regulatory Approval**" means all approvals, product or establishment licenses, registrations or authorizations of any Regulatory Agency necessary for the manufacture, use, storage, import, export, transport, offer for sale, or sale of any Product.

"**Related Parties**" means, with respect to any Person, such Person's Affiliates and the partners, directors, officers, employees, agents, trustees, administrators, managers, advisors and representatives of such Person and of such Person's Affiliates.

"**Release**" means any release, spill, emission, leaking, pumping, pouring, injection, escaping, deposit, disposal, discharge, dispersal, dumping, leaching or migration of any Hazardous Material into the indoor or outdoor environment (including the abandonment or disposal of any barrels, containers or other closed receptacles containing any Hazardous Material), including the movement of any Hazardous Material through the air, soil, surface water or groundwater, in each case, in the United States.

"**Required Lenders**" means, prior to the Closing Date, Lenders obligated with respect to greater than fifty percent (50%) of the Term Loan Commitments and, thereafter, Lenders representing greater than fifty percent (50%) of the outstanding principal amount of the Term Loans.

"**Requirements of Law**" means, as to any Person, the organizational or governing documents of such Person, and any law (statutory or common), treaty, order, policy, rule or regulation or determination of an arbitrator or a court or other Governmental Authority (including Health Care Laws, Data Protection Laws, FDA Laws, DEA Laws, and all applicable statutes, rules, regulations, standards, guidelines, policies and orders administered or issued by any foreign Governmental Authority), in each case, applicable to and binding upon such Person or any of its assets or properties or to which such Person or any of its assets or properties are subject.

"**Responsible Officers**" means, with respect to Borrower, collectively, the Chief Executive Officer, President, Chief Commercial Officer, Chief Medical Officer, Chief Compliance Officer, Chief Legal Officer and Chief Financial Officer of Borrower.

"**Restricted License**" means any material license or other agreement of the kind or nature subject or purported to be subject from time to time to a Lien under any Collateral Document, with respect to which a Credit Party is the licensee, (a) that prohibits or otherwise restricts such Credit Party from granting a security interest in such Credit Party's interest in such license or agreement in a manner enforceable under Requirements of Law, or (b) for which a breach of or default under could interfere with the Collateral Agent's or any Lender's right to sell any Collateral.

"**Sanctions**" is defined in Section 4.18(c).

"**SEC**" shall mean the Securities and Exchange Commission and any analogous Governmental Authority.

"**Secured Parties**" means each Lender, each other Indemnified Person and each other holder of any Obligation of a Credit Party.

"**Securities Account**" means any "securities account" as defined in the Code with such additions to such term as may hereafter be made.

"**Securities Act**" means the Securities Act of 1933.

"**Security Agreement**" means the Guaranty and Security Agreement, dated as of the Closing Date, by and among the Credit Parties and the Collateral Agent, in form and substance substantially similar to Exhibit C attached hereto or in such form or substance as the Credit Parties and the Collateral Agent may otherwise agree.

"**Solvent**" means, with respect to any Person as of any date of determination, that, as of such date, (a) the value of the assets (including goodwill minus disposition costs) of such Person (both at fair value and present fair saleable value), on a going concern basis, is greater than the total amount of liabilities (including contingent and unliquidated liabilities) of such Person, (b) such Person is able to generally pay all liabilities (including trade debt) of such Person as such liabilities become absolute and mature in the ordinary course of business consistent with past practice and (c) such Person does not have unreasonably small capital after giving due consideration to the prevailing practice in the industry in which it is engaged or will be engaged. In computing the amount of contingent or unliquidated liabilities at any time, such liabilities shall be computed at the amount that, in light of all the facts and circumstances existing at such time, represents the amount that can reasonably be expected to become an actual or matured liability.

"**Specified Disputes**" is defined in Section 4.7.

"**SSA**" means the Social Security Act of 1935, codified at Title 42, Chapter 7, of the United States Code.

"**Stock Acquisition**" means the purchase or other acquisition by Borrower or any of its Subsidiaries of all of the Equity Interests (by merger, stock purchase or otherwise) in any other Person.

"**Subordinated Debt**" means any Indebtedness in the form of or otherwise constituting term debt incurred by any Credit Party or any Subsidiary thereof (including any Indebtedness incurred in connection with any Acquisition or other Investment) that: (a) is subordinated in right of payment to the Obligations at all times until all of the Obligations have been paid, performed or discharged in full and Borrower has no further right to obtain any Credit Extension hereunder pursuant to a subordination, intercreditor or other similar agreement that is in form and substance reasonably satisfactory to the Collateral Agent (which agreement shall include turnover provisions that are reasonably satisfactory to the Collateral Agent); (b) except as permitted by clause (d) below, is not subject to scheduled amortization, redemption (mandatory), sinking fund or similar payment and does not have a final maturity, in each case, before a date that is at least one hundred and twenty (120) days following the Term Loan Maturity Date; (c) does not include covenants (including financial covenants) and agreements (excluding agreements with respect to maturity, amortization, pricing and other economic terms) that, taken as a whole, are more restrictive or onerous on the Credit Parties in any material respect than the comparable covenants and agreements, taken as a whole, in the Loan Documents (as reasonably determined by a Responsible Officer of Borrower in good faith); (d) is not subject to repayment or prepayment, including pursuant to a put option exercisable by the holder of any such Indebtedness, prior to a date that is at least one hundred and twenty (120) days following the final maturity thereof except in the case of an event of default or change of control (or the equivalent thereof, however described); and (e) does not provide or otherwise include provisions having the effect of providing that a default or event of default (or the equivalent thereof, however described) under or in respect of such Indebtedness shall exist, or such Indebtedness shall otherwise become due prior to its scheduled maturity or the holder or holders thereof or any trustee or agent on its or their behalf shall be permitted (with or without the giving of notice, the lapse of time or both) to cause any such Indebtedness to become due, or to require the prepayment, repurchase, redemption or defeasance thereof, prior to its scheduled maturity, in any such case upon the occurrence of a Default or Event of Default hereunder unless and until the Obligations have been declared, or have otherwise automatically become, immediately due and payable pursuant to Section 8.1(a).

"**Subsidiary**" means, with respect to any Person, a corporation, partnership, limited liability company or other entity of which more than fifty percent (50.0%) of whose shares of stock or other ownership interests having ordinary voting power (other than stock or such other ownership interests having such power only by reason of the happening of a contingency) to elect a majority of the Board of Directors (or similar body) of such corporation, partnership or other entity are at the time owned, directly or indirectly through one or more intermediaries, or both, by such Person. Unless the context otherwise requires, each reference to a Subsidiary herein shall be a reference to a Subsidiary of a Credit Party.

"**Tax**" means any present or future taxes, levies, imposts, duties, deductions, withholdings (including backup withholding), assessments, fees or other charges imposed by any Governmental Authority, including any interest, additions to tax or penalties applicable thereto.

"**Term Loan**" means each of the Tranche A Loan and the Tranche B Loan, as applicable, and "Term Loans" means, collectively, the Tranche A Loan and the Tranche B Loan (to the extent funded).

"**Term Loan Commitment**" mean each of the Tranche A Loan Commitment and the Tranche B Loan Commitment, as applicable, and "**Term Loan Commitments**" means, collectively, the Tranche A Loan Commitment and the Tranche B Loan Commitment.

"**Term Loan Maturity Date**" means the 72nd-month anniversary of the Tranche A Closing Date.

"**Term Loan Rate**" is defined in Section 2.3(a)(i).

"**Territory**" means, with respect to the Product, the world.

"**Third Party IP**" is defined in Section 4.6(l).

"**Trademark License**" means any agreement, whether written or oral, providing for the grant by or to a Person of any right to use any Trademark.

"**Trademarks**" means (a) all trademarks, trade names, corporate names, company names, business names, fictitious business names, service marks, elements of package or trade dress of goods or services, logos and other source or business identifiers, together with the goodwill associated therewith, all registrations and recordings thereof, and all applications in connection therewith, in the United States Patent and Trademark Office or in any similar office or agency of the United States or any state thereof or in any similar office or agency anywhere in the world in which foreign counterparts are registered or issued, and (b) all renewals thereof.

"**Tranche A Closing Date**" means the date on which the Tranche A Loan is advanced by Lenders, which, subject to the satisfaction of the conditions precedent to the Tranche A Loan set forth in Section 3.1, Section 3.3 and Section 3.5, shall be ten (10) Business Days following the Effective Date.

"**Tranche A Commitment**" means, with respect to any Lender, the commitment of such Lender to make the Credit Extensions relating to the Tranche A Loan on the Tranche A Closing Date in the aggregate principal amount set forth opposite such Lender's name on Exhibit D attached hereto.

"**Tranche A Loan**" is defined in Section 2.2(a)(i).

"**Tranche A Loan Amount**" means an original principal amount equal to Seventy-Five Million Dollars ($75,000,000.00).

"**Tranche A Makewhole Amount**" means, as of any date of determination occurring prior to the 3rd-year anniversary of the Tranche A Closing Date, an amount equal to the sum of all interest that would have accrued and been payable from such date through the 3rd-year anniversary of the Tranche A Closing Date.

"**Tranche A Note**" means a promissory note in substantially the form attached hereto as Exhibit B-1, as it may be amended, restated, supplemented or otherwise modified from time to time.

"**Tranche A Prepayment Premium**" means, with respect to any prepayment of the Tranche A Loan by Borrower pursuant to Section 2.2(c) or as a result of the acceleration of the maturity of the Term Loans pursuant to Section 8.1(a), an amount equal to the product of the amount of any principal so prepaid, multiplied by:

(a) if such prepayment occurs prior to the 3rd-year anniversary of the Tranche A Closing Date, 0.03;

(b) if such prepayment occurs on or after the 3rd -year anniversary of the Tranche A Closing Date but prior to the 4th-year anniversary of the Tranche A Closing Date, 0.02; and

(c) if such prepayment occurs on or after the 4th-year anniversary of the Tranche A Closing Date Tranche A Closing Date but prior to the 5th-year anniversary of the Tranche A Closing Date, 0.01.

For the avoidance of doubt, no Tranche A Prepayment Premium shall be due and owing for any payment of principal of the Tranche A Loan made on the Term Loan Maturity Date.

"**Tranche B Closing Date**" means the date on which the Tranche B Loan is advanced by Lenders, which, at Borrower's option and as indicated in the Payment/Advance Request for the Tranche B Loan and subject to the satisfaction of the conditions precedent to the Tranche B Loan set forth in Section 3.2, Section 3.3 and Section 3.5, shall be ninety (90) days (or such shorter period as may be agreed to by Lenders) following the delivery by Borrower to Collateral Agent of a completed Payment/Advance Request in the form of Exhibit A hereto for the Tranche B Loan and, in no event, later than December 31, 2020.

"**Tranche B Commitment**" means, with respect to any Lender, the commitment of such Lender to make the Credit Extensions relating to the Tranche B Loan on the Tranche B Closing Date in the aggregate principal amount set forth opposite such Lender's name on Exhibit D attached hereto; provided, however, that the parties hereto agree that such commitment, and any obligations of such Lender hereunder with respect thereto, shall terminate automatically without any further action by any party hereto and be of no further force and effect if (x) any prepayment of the Tranche A Loan is made, in whole or in part, on or before the Tranche B Closing Date or (y) Borrower does not timely deliver a Payment/Advance Request to the Collateral Agent on or before June 30, 2020 with respect to the request to fund the Tranche B Loan Amount on a Tranche B Closing Date (in either of which case, for purposes of this Agreement, such Lender's Tranche B Commitment would become zero).

"**Tranche B Loan**" is defined in Section 2.2(a)(ii).

"**Tranche B Loan Amount**" means an original principal amount equal to Seventy-Five Million Dollars $75,000,000.00).

"**Tranche B Makewhole Amount**" means, as of any date of determination occurring prior to the 3rd-year anniversary of the Tranche B Closing Date, an amount equal to the sum of all interest that would have accrued and been payable from such date through the 3rd year anniversary of the Tranche B Closing Date.

"**Tranche B Note**" means a promissory note in substantially the form attached hereto as Exhibit B-2, as it may be amended, restated, supplemented or otherwise modified from time to time.

"**Tranche B Prepayment Premium**" means, with respect to any prepayment of the Tranche B Loan by Borrower pursuant to Section 2.2(c) or as a result of the acceleration of the maturity of the Term Loans pursuant to Section 8.1(a), an amount equal to the product of the amount of any principal so prepaid, multiplied by:

(a) if such prepayment occurs prior to the 3rd-year anniversary of the Tranche B Closing Date, 0.03;

(b) if such prepayment occurs on or after the 3rd-year anniversary of the Tranche B Closing Date but prior to the 4th-year anniversary of the Tranche A Closing Date, 0.02; and

(c) if such prepayment occurs on or after the 4th-year anniversary of the Tranche B Closing Date Tranche A Closing Date but prior to the 5th-year anniversary of the Tranche A Closing Date, 0.01.

"**Transfer**" is defined in Section 6.1.

"**Treasury Regulations**" mean those regulations promulgated pursuant to the IRC.

"**TRICARE**" means, collectively, a program of medical benefits covering former and active members of the uniformed services and certain of their dependents, financed and administered by the United States Departments of Defense, Health and Human Services and Transportation, and all laws applicable to such programs.

"**UKBA**" is defined in Section 4.18(a).

"**United States**" or "**U.S.**" means the United States of America, its fifty (50) states, the District of Columbia and Puerto Rico.

"**Wholly-Owned Subsidiary**" means, with respect to any Person, a Subsidiary of such Person, all of the Equity Interests of which (other than directors' qualifying shares or nominee or other similar shares required pursuant to Requirements of Law) are owned by such Person or another Wholly-Owned Subsidiary of such Person. Unless the context otherwise requires, each reference to a Wholly-Owned Subsidiary herein shall be a reference to a Wholly-Owned Subsidiary of a Credit Party.

"**Withdrawal Liability**" means liability to a Multiemployer Plan as a result of a complete or partial withdrawal from such Multiemployer Plan, as such terms are defined in Part I of Subtitle E of Title IV of ERISA.

[Signature page follows.]

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed as of the Effective Date.

GLOBAL BLOOD THERAPEUTICS, INC.,
as Borrower

By: /s/ Jeffrey Farrow
Name: Jeffrey Farrow
Title: Chief Financial Officer

BIOPHARMA CREDIT PLC,
as Collateral Agent and Lender

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By: /s/ Pedro Gonzalez de Cosio
Name: Pedro Gonzalez de Cosio
Title: Managing Member

BIOPHARMA CREDIT PLC INVESTMENTS V (MASTER) LP,
as Lender

By: Pharmakon Advisors, LP,
its Investment Manager
By: Pharmakon Management I, LLC,
its General Partner

By: /s/ Pedro Gonzalez de Cosio
Name: Pedro Gonzalez de Cosio
Title: CEO and Managing Member

EXHIBIT A – PAYMENT/ADVANCE REQUEST FORM

The undersigned, being the duly elected and acting of GLOBAL BLOOD THERAPEUTICS, INC., a Delaware corporation ("**Borrower**"), does hereby certify, solely in his/her capacity as an authorized officer of Borrower and not in his/her personal capacity, to each of BIOPHARMA CREDIT PLC (in its capacity as "Collateral Agent" and a "Lender") and BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP (a "Lender"), in connection with that certain Loan Agreement dated as of _____, 2019 by and among Borrower, Lenders and the other parties thereto (the "Loan Agreement"; with other capitalized terms used below having the meanings ascribed thereto in the Loan Agreement) that, subject to the satisfaction (or waiver by Required Lenders) of the conditions precedent to the Tranche [A] [B] Loan set forth in Section 3 of the Loan Agreement, on [the Tranche A Closing Date] [[_____, 20__] (the "Tranche B Closing Date")]:

1. the representations and warranties made by the Credit Parties in Section 4 of the Loan Agreement and in the other Loan Documents are true and correct in all material respects, unless any such representation or warranty is stated to relate to a specific earlier date, in which case such representation or warranty shall be true and correct in all material respects as of such earlier date (it being understood that any representation or warranty that is qualified as to "materiality," "Material Adverse Change," or similar language shall be true and correct in all respects on the Tranche [A][B] Closing Date[3] or as of such earlier date, as applicable);

2. no Default or Event of Default has occurred since the [Effective Date][4] [Tranche A Closing Date][5] or is occurring as of the date hereof;

3. each of the Credit Parties is in compliance with the covenants and requirements contained in Sections 5 and 6 of the Loan Agreement;

4. all conditions referred to in Section 3 of the Loan Agreement to the making of the Tranche [A][B] Loan[6] to be made on the Tranche [A][B] Closing Date[7] have been satisfied (or waived in writing by the Required Lenders);

5. no Material Adverse Change has occurred since the [Effective Date][8] [Tranche A Closing Date][9];

6. the undersigned is a Responsible Officer of Borrower; and

7. the proceeds of the [Tranche A Loan][10] [Tranche B Loan][11] shall be disbursed as set forth on Attachment A hereto[12].

Dated: _____, 20__[13]

3 As applicable.
4 To be included in Payment/Advance Form for Tranche A Loan only.
5 To be included in Payment/Advance Form for Tranche B Loan only.
6 As applicable.
7 As applicable.
8 To be included in Payment/Advance Form for Tranche A Loan only.
9 To be included in Payment/Advance Form for Tranche B Loan only.
10 To be included in Payment/Advance Form for Tranche A Loan only.
11 To be included in Payment/Advance Form for Tranche B Loan only.
12 To be prepared in coordination with Lender (or Lender's counsel).
13 In Payment/Advance Form for Tranche B Loan, insert date no later than 15 days prior to the Tranche B Closing Date.

[Signature page follows]

GLOBAL BLOOD THERAPEUTICS, INC.,
as Borrower
By _____
Name: _____
Title: _____

EXHIBIT B-1

THIS NOTE CONTAINS ORIGINAL ISSUE DISCOUNT, AS DEFINED IN SECTION 1273 OF THE INTERNAL REVENUE CODE OF 1986 AS AMENDED. PLEASE CONTACT [_____], CHIEF FINANCIAL OFFICER, [address], TELEPHONE: [_____] TO OBTAIN INFORMATION REGARDING THE ISSUE PRICE OF THE NOTE, THE AMOUNT OF ORIGINAL ISSUE DISCOUNT IN THE NOTE AND THE YIELD TO MATURITY.

TRANCHE A NOTE

$75,000,000.00 Dated: [_____], 2019

FOR VALUE RECEIVED, the undersigned, GLOBAL BLOOD THERAPEUTICS, INC., a Delaware corporation ("**Borrower**"), HEREBY PROMISES TO PAY to [BIOPHARMA CREDIT PLC] [BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP] ("**Lender**"), or its registered assignees, the principal amount of SEVENTY-FIVE MILLION DOLLARS ($75,000,000.00), plus interest on the aggregate unpaid principal amount hereof at a per annum rate equal to the LIBOR Rate plus Seven percent (7.00%) per annum, and in accordance with the terms of the Loan Agreement dated as of _____, 2019 by and among Borrower, Lender and the other parties thereto (as may be amended, restated, supplemented or otherwise modified from time to time, the "**Loan Agreement**"). If not sooner paid, the entire principal amount, all accrued and unpaid interest hereunder, all due and unpaid Lender Expenses and any other amounts payable under the Loan Documents shall be due and payable on the Term Loan Maturity Date. Any capitalized term not otherwise defined herein shall have the meaning attributed to such term in the Loan Agreement.

Borrower shall make equal quarterly payments of principal of the Tranche A Loan commencing on the first Payment Date on or immediately following the 39th-month anniversary of the Tranche A Closing Date. All unpaid principal with respect to the Tranche A Loan (and, for the avoidance of doubt, all accrued and unpaid interest, all due and unpaid Lender Expenses and any other amounts payable under the Loan Documents) is due and payable in full on the Term Loan Maturity Date. Interest shall accrue on this Tranche A Note commencing on, and including, the date of this Tranche A Note, and shall accrue on this Tranche A Note, or any portion thereof, for the day on which this Tranche A Note or such portion is paid. Interest on this Tranche A Note shall be payable in accordance with Section 2.3 of the Loan Agreement.

Principal, interest and all other amounts due with respect to this Tranche A Note are payable in lawful money of the United States of America to Lender as set forth in the Loan Agreement and this Tranche A Note.

The Loan Agreement, among other things, (a) provides for the making of secured Term Loans by Lender to Borrower, and (b) contains provisions for acceleration of the maturity hereof upon the happening of certain stated events.

This Tranche A Note may not be prepaid except as set forth in Section 2.2(c) of the Loan Agreement or as expressly provided in Section 8.1 of the Loan Agreement.

This Tranche A Note and the obligation of Borrower to repay the unpaid principal amount of this Tranche A Note, interest thereon, and all other amounts due Lender under the Loan Agreement are secured pursuant to the Collateral Documents.

Presentment for payment, demand, notice of protest and all other demands and notices of any kind in connection with the execution, delivery, performance and enforcement of this Tranche A Note are hereby waived.

THIS TRANCHE A NOTE SHALL BE GOVERNED BY, AND CONSTRUED AND INTERPRETED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK, WITHOUT REGARD TO ANY PRINCIPLES OF CONFLICTS OF LAW THAT COULD REQUIRE THE APPLICATION OF THE LAW OF ANY OTHER JURISDICTION.

Note Register; Ownership of Note. The ownership of an interest in this Tranche A Note shall be registered on a record of ownership maintained by the Collateral Agent. Notwithstanding anything else in this Tranche A Note to the contrary, the right to the principal of, and stated interest on, this Tranche A Note may be transferred only if the transfer is registered on such record of ownership and the transferee is identified as the owner of an interest in the obligation. Borrower shall be entitled to treat the registered holder of this Tranche A Note (as recorded on such record of ownership) as the owner in fact thereof for all purposes and shall not be bound to recognize any equitable or other claim to or interest in this Tranche A Note on the part of any other Person.

IN WITNESS WHEREOF, Borrower has caused this Tranche A Note to be duly executed by one of its officers thereunto duly authorized on the date hereof.

BORROWER:

GLOBAL BLOOD THERAPEUTICS, INC.,
as Borrower

By: _____
Name: _____
Title: _____

EXHIBIT B-2

THIS NOTE CONTAINS ORIGINAL ISSUE DISCOUNT, AS DEFINED IN SECTION 1273 OF THE INTERNAL REVENUE CODE OF 1986 AS AMENDED. PLEASE CONTACT [_____], CHIEF FINANCIAL OFFICER, [address], TELEPHONE: [_____] TO OBTAIN INFORMATION REGARDING THE ISSUE PRICE OF THE NOTE, THE AMOUNT OF ORIGINAL ISSUE DISCOUNT IN THE NOTE AND THE YIELD TO MATURITY.

TRANCHE B NOTE

$75,000,000.00 Dated: [_____], 20__

FOR VALUE RECEIVED, the undersigned, GLOBAL BLOOD THERAPEUTICS, INC. , a Delaware corporation ("**Borrower**"), HEREBY PROMISES TO PAY to [BIOPHARMA CREDIT PLC] [BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP] ("**Lender**"), or its registered assignees, the principal amount of SEVENTY-FIVE MILLION DOLLARS ($75,000,000.00), plus interest on the aggregate unpaid principal amount hereof at a per annum rate equal to the LIBOR Rate plus Seven percent (7.00%) per annum, and in accordance with the terms of the Loan Agreement dated as of _____, 2019 by and among Borrower, Lender and the other parties thereto (as may be amended, restated, supplemented or otherwise modified from time to time, the "**Loan Agreement**"). If not sooner paid, the entire principal amount, all accrued and unpaid interest hereunder, all due and unpaid Lender Expenses and any other amounts payable under the Loan Documents shall be due and payable on the Term Loan Maturity Date. Any capitalized term not otherwise defined herein shall have the meaning attributed to such term in the Loan Agreement.

Borrower shall make equal quarterly payments of principal of the Tranche B Loan commencing on the first Payment Date on or immediately following the 39th-month anniversary of the Tranche B Closing Date. All unpaid principal with respect to the Tranche B Loan (and, for the avoidance of doubt, all accrued and unpaid interest, all due and unpaid Lender Expenses and any other amounts payable under the Loan Documents) is due and payable in full on the Term Loan Maturity Date. Interest shall accrue on this Tranche B Note commencing on, and including, the date of this Tranche B Note, and shall accrue on this Tranche A Note, or any portion thereof, for the day on which this Tranche B Note or such portion is paid. Interest on this Tranche B Note shall be payable in accordance with Section 2.3 of the Loan Agreement.

Principal, interest and all other amounts due with respect to this Tranche B Note are payable in lawful money of the United States of America to Lender as set forth in the Loan Agreement and this Tranche B Note.

The Loan Agreement, among other things, (a) provides for the making of secured Term Loans by Lender to Borrower, and (b) contains provisions for acceleration of the maturity hereof upon the happening of certain stated events.

This Tranche B Note may not be prepaid except as set forth in Section 2.2(c) of the Loan Agreement or as expressly provided in Section 8.1 of the Loan Agreement.

This Tranche B Note and the obligation of Borrower to repay the unpaid principal amount of this Tranche B Note, interest thereon, and all other amounts due Lender under the Loan Agreement are secured pursuant to the Collateral Documents.

Presentment for payment, demand, notice of protest and all other demands and notices of any kind in connection with the execution, delivery, performance and enforcement of this Tranche B Note are hereby waived.

THIS TRANCHE B NOTE SHALL BE GOVERNED BY, AND CONSTRUED AND INTERPRETED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK, WITHOUT REGARD TO ANY PRINCIPLES OF CONFLICTS OF LAW THAT COULD REQUIRE THE APPLICATION OF THE LAW OF ANY OTHER JURISDICTION.

Note Register; Ownership of Note. The ownership of an interest in this Tranche B Note shall be registered on a record of ownership maintained by the Collateral Agent. Notwithstanding anything else in this Tranche B Note to the contrary, the right to the principal of, and stated interest on, this Tranche B Note may be transferred only if the transfer is registered on such record of ownership and the transferee is identified as the owner of an interest in the obligation. Borrower shall be entitled to treat the registered holder of this Tranche B Note (as recorded on such record of ownership) as the owner in fact thereof for all purposes and shall not be bound to recognize any equitable or other claim to or interest in this Tranche B Note on the part of any other Person.

IN WITNESS WHEREOF, Borrower has caused this Tranche B Note to be duly executed by one of its officers thereunto duly authorized on the date hereof.

BORROWER:

GLOBAL BLOOD THERAPEUTICS, INC.,
as Borrower

By: _____
Name: _____
Title: _____

EXHIBIT C

FORM OF SECURITY AGREEMENT

GUARANTY AND SECURITY AGREEMENT

Dated as of [_____], 2019

by

GLOBAL BLOOD THERAPEUTICS, INC.

(as *Borrower*),

THE GUARANTORS PARTY HERETO,

and

EACH OTHER GRANTOR
FROM TIME TO TIME PARTY HERETO

in favor of

BIOPHARMA CREDIT PLC

(as *Collateral Agent* on behalf of Lenders and the other Secured Parties)

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(continued)

GUARANTY AND SECURITY AGREEMENT, dated as of [_____], 2019, by GLOBAL BLOOD THERAPEUTICS, INC., a Delaware corporation ("Borrower"), the Guarantors party to the Loan Agreement (as defined below) as of the date hereof, and each other Person that becomes a party hereto pursuant to Section 8.6 (together with Borrower and such Guarantors, "Grantors"), in favor of BIOPHARMA CREDIT PLC, a public limited company incorporated under the laws of England and Wales (as the "Collateral Agent") on behalf of Lenders and each other Secured Party.

W I T N E S S E T H:

WHEREAS, pursuant to the Loan Agreement dated as of December 17, 2019 (as the same may be amended, restated, amended and restated, supplemented or otherwise modified from time to time, the "Loan Agreement") by and among Borrower, the Collateral Agent and the other parties thereto, Lenders agrees to make extensions of credit to Borrower upon the terms and subject to the conditions set forth therein;

WHEREAS, each Grantor other than Borrower agrees to guaranty, jointly and severally, the Obligations (as defined in the Loan Agreement) of Borrower;

WHEREAS, each Grantor will derive substantial direct and indirect benefits from the making of the extensions of credit under the Loan Agreement; and

WHEREAS, it is a condition precedent to the obligation of Lenders to extend credit to Borrower under the Loan Agreement that the Grantors shall have executed and delivered this Agreement to the Collateral Agent and each Lender for the benefit of Lenders and the other Secured Parties.

NOW, THEREFORE, in consideration of the mutual premises herein contained and for valuable consideration the receipt and sufficiency of which is hereby acknowledged and to induce the Collateral Agent, Lenders and the Credit Parties to enter into the Loan Agreement and to induce each Lender to make extensions of credit to Borrower thereunder, each Grantor hereby agrees with the Collateral Agent, each intending to be legally bound, as follows:

ARTICLE I

DEFINED TERMS

Section 1.1.Definitions. Capitalized terms used herein without definition are used as defined in the Loan Agreement.

(a) The following terms have the meanings given to them in the Code and terms used herein without definition that are defined in the Code have the meanings given to them in the Code (such meanings to be equally applicable to both the singular and plural forms of the terms defined): "account", "account debtor", "as-extracted collateral", "certificated security", "chattel paper", "check", "commercial tort claim", "commodity account", "commodity contract", "documents", "deposit account", "electronic chattel paper", "encumbrance", "entitlement holder", "equipment", "farm products", "financial asset", "fixture", "general intangible", "goods", "health-care-insurance receivable", "instruments", "inventory", "investment property", "letter of credit", "letter-of-credit right", "money", "proceeds", "promissory note", "record", "securities account", "security", "security entitlement", "supporting obligation", "tangible chattel paper" and "uncertificated security".

(b) The following terms shall have the following meanings:

"Agreement" means this Guaranty and Security Agreement, as it may be amended, restated, supplemented or otherwise modified from time to time.

"Applicable IP Office" means the United States Patent and Trademark Office or the United States Copyright Office.

"Collateral" has the meaning specified in Section 3.1.

"Excluded Property" means, collectively:

(i) any "intent to use" United States Trademark applications for which a statement of use or an amendment to allege use has not been filed (but only until such statement is filed) solely to the extent, if any, that, and only during the period, if any, in which, the grant of a security interest therein would impair the validity or enforceability of such intent to use Trademark applications under applicable federal law;

(ii) any permit, lease, license, contract, instrument or other agreement held by any Grantor with respect to which, the grant to the Collateral Agent, in favor of and for the benefit of Lenders and the other Secured Parties, of a security interest therein and Lien thereupon, and the pledge to the Collateral Agent thereof, in favor of and for the benefit of Lenders and the other Secured Parties, to secure the Obligations (and any guaranty thereof) are validly prohibited by the terms thereof, but only, in each case, to the extent, and for so long as, such prohibition is not terminated or rendered unenforceable or otherwise deemed ineffective by the Code (including Sections 9-406(d), 9-407(a), 9-408(a) and 9-409 of the Code) or by any applicable Requirements of Law;

(iii) any other permit, lease, license, contract, instrument or other agreement held by any Grantor with respect to which, the grant to the Collateral Agent, in favor of and for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien thereupon, and the pledge to the Collateral Agent thereof, in favor of and for the benefit of Lenders and the other Secured Parties, to secure the Obligations (and any guaranty thereof) require the consent, approval or waiver of any Governmental Authority or other third party (other than Borrower or an Affiliate of Borrower) and such consent, approval or waiver has not been obtained by such Grantor or Borrower following their respective commercially reasonable efforts to obtain the same;

(iv) any other asset or property subject or purported to be subject to a Lien under any Collateral Document held by any Grantor with respect to which, the grant to the Collateral Agent, in favor of and for the benefit of Lenders and the other Secured Parties, of a security interest in and Lien thereupon, and the pledge to the Collateral Agent thereof, in favor of and for the benefit of Lenders and the other Secured Parties, to secure the Obligations (and any guaranty thereof) require the consent, approval or waiver of any Governmental Authority or other third party (other than Borrower or an Affiliate of Borrower) and such consent, approval or waiver has not been obtained by such Grantor or Borrower following their respective commercially reasonable efforts to obtain the same;

(v) any property or asset subject or purported to be subject to a Lien under any Collateral Document held by any Grantor that is a non-Wholly-Owned Subsidiary with respect to which, the grant to the Collateral Agent, in favor of and for the benefit of Lenders and the other Secured Parties, of a security interest therein and Lien thereupon, and the pledge to the Collateral Agent thereof, in favor of and for the benefit of Lenders and the other Secured Parties, to secure the Obligations (and any guaranty thereof) are validly prohibited by, or would give any third party (other than Borrower or an Affiliate of Borrower) the right to terminate its obligations under, the Operating Documents of, the joint venture agreement or shareholder agreement with respect to, or any other contract with such third party relating to such non-Wholly-Owned Subsidiary (other than customary non-assignment provisions which are ineffective under Article 9 of the Code or other Requirements of Law), but only, in each case, to the extent, and for so long as such Operating Documents, joint venture agreement, shareholder agreement or other contract is in effect;

(vi) any asset or property subject or purported to be subject to a Lien under any Collateral Document held by any Grantor with respect to which, the cost, difficulty, burden or consequences (including adverse Tax consequences) of granting the Collateral Agent, in favor of and for the benefit of Lenders and the other Secured Parties, a security interest therein and Lien thereupon, and pledging to the Collateral Agent thereof, in favor of and for the benefit of Lenders and the other Secured Parties, to secure the Obligations (and any guaranty thereof) are excessive relative to the value to be afforded to Lenders thereby;

(vii) any rights under any Federal or state governmental license, permit, franchise or authorization to the extent that the granting of a security interest therein is specifically prohibited or restricted by any Requirements of Law;

(viii) any asset or property subject to a Permitted Lien to the extent the documents governing such Permitted Lien or the Permitted Indebtedness secured thereby validly prohibit other Liens on such assets or property, but only, in each case, to the extent, and for so long as, such prohibition is not terminated or rendered unenforceable or otherwise deemed ineffective by the Code (including Sections 9-406(d), 9-407(a), 9-408(a) and 9-409 of the Code) or by any applicable Requirements of Law;

(ix) leasehold interests in real property;

(x) fee interests in real property with a fair market value (reasonably determined in good faith by a Responsible Officer of Borrower) less than $5,000,000;

(xi) Vehicles;

(xii) any letter of credit with an amount less than $500,000 and all letter-of-credit rights with respect thereto;

(xiii) any other property or assets (other than Intellectual Property) as to which the creation or attachment of a lien is not governed by Article 9 of the Code;

(xiv) any Intellectual Property unrelated in any way to the research, development, manufacture, production, use, commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of any Product in the Territory, including any similar or equivalent rights to those set forth in clauses (a) through (f) of the definition of "Intellectual Property";

(xv) Excluded Equity Interests; and

(xvi) Excluded Accounts;

provided, however, that "Excluded Property" shall not include any proceeds, products, substitutions or replacements of Excluded Property (unless such proceeds, products, substitutions or replacements would otherwise constitute Excluded Property).

"Fraudulent Transfer Laws" has the meaning set forth in Section 2.2.

"Guaranteed Obligations" has the meaning set forth in Section 2.1.

"Guarantor" means each Grantor other than Borrower.

"Guaranty" means the guaranty of the Guaranteed Obligations made by Guarantors as set forth in this Agreement.

"IP License" means all express and implied grants or rights to make, have made, use, sell, reproduce, distribute, modify, or otherwise exploit any Intellectual Property, as well as all covenants not to sue and co-existence agreements (and all related IP Ancillary Rights), whether written or oral, relating to any Intellectual Property.

"Maximum Guaranteed Amount" has the meaning set forth in Section 2.2.

"NDA" means a new drug application filed with the FDA pursuant to Section 505(b) of the U.S. Federal Food, Drug, and Cosmetic Act, along with all supplements and amendments thereto.

"Pledged Certificated Stock" means all of the Equity Interests (other than Excluded Equity Interests) of any Subsidiary evidenced by a certificate, instrument or other similar document (as defined in the Code), in each case owned by any Grantor, including a Grantor's right, title and interest resulting from its ownership of any such Equity Interests as a limited or general partner in any partnership that has issued Pledged Certificated Stock or as a member of any limited liability company that has issued Pledged Certificated Stock, and a Grantor's right, title and interest resulting from its ownership of any such Equity Interests in, to and under any Operating Document or shareholder agreement of any corporation, partnership or limited liability company to which it is a party, and any distribution of property made on, in respect of or in exchange for the foregoing from time to time, including all certificated Equity Interests listed on Schedule 1 of the Security Disclosure Letter. "Pledged Certificated Stock" includes, for the avoidance of doubt, any Pledged Uncertificated Stock that subsequently becomes certificated.

"Pledged Collateral" means, collectively, the Pledged Stock and the Pledged Debt Instruments.

"Pledged Debt Instruments" means all right, title and interest of any Grantor in instruments evidencing any Indebtedness owed to such Grantor or other obligations owed to such Grantor, and any distribution of property made on, in respect of or in exchange for the foregoing from time to time, including all Indebtedness described on Schedule 3 of the Security Disclosure Letter, issued by the obligors named therein. "Pledged Debt Instruments" excludes any Excluded Property.

"Pledged Investment Property" means any investment property of any Grantor, and any distribution of property made on, in respect of or in exchange for the foregoing from time to time, other than any Pledged Stock or Pledged Debt Instruments. "Pledged Investment Property" excludes any Excluded Property.

"Pledged Stock" means all Pledged Certificated Stock and all Pledged Uncertificated Stock.

"Pledged Uncertificated Stock" means all of the Equity Interests (other than Excluded Equity Interests) of any Subsidiary that is not Pledged Certificated Stock, in each case owned by any Grantor, including Grantor's right, title and interest resulting from its ownership of any such Equity Interests as a limited or general partner in any partnership not constituting Pledged Certificated Stock or as a member of any limited liability company not constituting Pledged Certificated Stock, a Grantor's right, title and interest resulting from its ownership of any such Equity Interests in, to and under any Operating Document or shareholder agreement of any partnership or limited liability company to which it is a party, and any distribution of property made on, in respect of or in exchange for the foregoing from time to time, including in each case those interests set forth on Schedule 1 of the Security Disclosure Letter, to the extent such interests are not certificated.

"Secured Obligations" has the meaning set forth in Section 3.2.

"Security Disclosure Letter" means the security agreement disclosure letter, dated as of the date hereof, delivered by the Grantors to the Collateral Agent and each Lender.

"Vehicles" means rolling stock, motor vehicles, vessels, aircraft and other assets subject to certificates of title.

Section 1.2. Certain Other Terms.

(a) For the purposes of and as used in this Agreement: (i) references to any Person include its successors and assigns and, in the case of any Governmental Authority, any Person succeeding to its functions and capacities; (ii) each authorization herein shall be deemed irrevocable and coupled with an interest; and (iii) where the context requires, provisions relating to any Collateral when used in relation to a Grantor shall refer to such Grantor's Collateral or any relevant part thereof.

(b) Other Interpretive Provisions.

(i) Defined Terms. Unless otherwise specified herein or therein, all terms defined in this Agreement shall have the defined meanings when used in any certificate or other document made or delivered pursuant hereto.

(ii) This Agreement. The words “hereof”, “herein”, “hereunder” and words of similar import when used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement.

(iii) Certain Common Terms. The words “include”, “included” and “including” are not limiting and mean “including without limitation.” The word “or” has the inclusive meaning represented by the phrase “and/or”. The word “shall” is mandatory. The word “may” is permissive. The singular includes the plural and the plural includes the singular.

(iv) Performance; Time. Whenever any performance obligation hereunder (other than a payment obligation) shall be stated to be due or required to be satisfied on a day other than a Business Day, such performance shall be made or satisfied on the next succeeding Business Day. In the computation of periods of time from a specified date to a later specified date, the word “from” means “from and including”; the words “to” and “until” each mean “to but excluding”, and the word “through” means “to and including.” If any provision of this Agreement refers to any action taken or to be taken by any Person, or which such Person is prohibited from taking, such provision shall be interpreted to encompass any and all means, direct or indirect, of taking, or not taking, such action.

(v) Contracts. Except as the context otherwise requires (including to the extent otherwise expressly provided herein), references to any contract, agreement, instrument or other document, including this Agreement and the other Loan Documents, shall be deemed to include any and all amendments, supplements or modifications thereto or restatements or substitutions thereof, in each case which are in effect from time to time, but only to the extent such amendments, supplements, modifications, restatements or substitutions are not prohibited by the terms of any Loan Document.

(vi) Laws. Except as the context otherwise requires (including to the extent otherwise expressly provided herein), references to any law, statute, treaty, order, policy, rule or regulation include any amendments, supplements and successors thereto, and references to any law, statute, treaty, order, policy, rule or regulation are to be construed as including all statutory and regulatory provisions related thereto or consolidating, amending, replacing, supplementing or interpreting such law, statute, treaty, order, policy, rule or regulation.

(vii) Excluded Property. Notwithstanding anything to the contrary herein, the representations, warranties and covenants set forth herein in relation to the assets of the Grantors shall not apply to any Excluded Property.

ARTICLE II

GUARANTY

Section 2.1. Guaranty. To induce Lenders to make the Term Loans to Borrower in accordance with the terms and conditions of the Loan Agreement, each Guarantor, jointly and severally with each other Guarantor, absolutely, unconditionally and irrevocably guarantees, as primary obligor and not merely as surety, the full and punctual payment when due, whether at stated maturity or earlier, by reason of acceleration, mandatory prepayment or otherwise in accordance with any Loan Document, of all the Obligations of Borrower existing on the date hereof or hereinafter incurred or created (the "Guaranteed Obligations"). This Guaranty by each Guarantor hereunder constitutes a guaranty of payment and not of collection. Each Guarantor hereby acknowledges and agrees that the Guaranteed Obligations, at any time and from time to time, may exceed the Maximum Guaranteed Amount of such Guarantor and may exceed the aggregate of the Maximum Guaranteed Amounts of all Guarantors, in each case without discharging, limiting or otherwise affecting the obligations of any Guarantor hereunder or the rights, powers and remedies of any Secured Party hereunder or under any other Loan Document.

Section 2.2. Limitation of Guaranty. Any term or provision of this Guaranty or any other Loan Document to the contrary notwithstanding, the maximum aggregate amount for which any Guarantor shall be liable hereunder (the "Maximum Guaranteed Amount") shall not exceed the maximum amount for which such Guarantor can be liable without rendering this Guaranty or any other Loan Document, as it relates to such Guarantor, subject to avoidance under applicable Requirements of Law relating to fraudulent conveyance or fraudulent transfer (including the Uniform Fraudulent Conveyance Act, the Uniform Fraudulent Transfer Act and Section 548 of title 11 of the United States Code or any applicable provisions of comparable Requirements of Law) (collectively, "Fraudulent Transfer Laws"). Any analysis of the provisions of this Guaranty for purposes of Fraudulent Transfer Laws shall take into account the right of contribution established in Section 2.7 below and, for purposes of such analysis, give effect to any discharge of intercompany debt as a result of any payment made under the Guaranty.

Section 2.3. Authorization; Other Agreements. The Collateral Agent, on behalf of Lenders and the other Secured Parties is hereby authorized, without notice, to or demand upon any Guarantor and without discharging or otherwise affecting the obligations of any Guarantor hereunder and without incurring any liability hereunder, from time to time, to do each of the following but subject in all cases to the terms and conditions of the other Loan Documents:

(a) subject to compliance with Section 11.5 of the Loan Agreement and Section 8.5 hereof (as applicable), (i) modify, amend, supplement or otherwise change, (ii) accelerate or otherwise change the time of payment or (iii) waive or otherwise consent to noncompliance with, any Guaranteed Obligation or any Loan Document;

(b) apply to the Guaranteed Obligations any sums by whomever paid or however realized to any Guaranteed Obligation in such order as provided in the Loan Documents;

(c) refund at any time any payment received by any Secured Party in respect of any Guaranteed Obligation;

(d) (i) sell, exchange, enforce, waive, substitute, liquidate, terminate, release, abandon, fail to perfect, subordinate, accept, substitute, surrender, exchange, affect, impair or otherwise alter or release any Collateral for any Guaranteed Obligation or any other guaranty therefor in any manner, (ii) receive, take and hold additional Collateral to secure any Guaranteed Obligation, (iii) add, release or substitute any one or more other Guarantors, makers or endorsers of any Guaranteed Obligation or any part thereof and (iv) otherwise deal in any manner with Borrower or any other Guarantor, maker or endorser of any Guaranteed Obligation or any part thereof; and

(e) settle, release, compromise, collect or otherwise liquidate the Guaranteed Obligations.

Section 2.4. Guaranty Absolute and Unconditional. Each Guarantor hereby waives and agrees not to assert any defense (other than the indefeasible payment in full of the Guaranteed Obligations (other than inchoate indemnity obligations)), whether arising in connection with or in respect of any of the following clauses (a) through (f) or otherwise, and hereby agrees that its obligations under this Guaranty are irrevocable, absolute and unconditional and shall not be discharged as a result of or otherwise affected by any of the following clauses (a) through (f) (which may not be pleaded and evidence of which may not be introduced in any proceeding with respect to this Guaranty, in each case except as otherwise agreed in writing by Lender):

(a) the invalidity or unenforceability of any obligation of Borrower or any other Guarantor under any Loan Document or any other agreement or instrument relating thereto (including any amendment, consent or waiver thereto), or any security for, or other guaranty of, any Guaranteed Obligation or any part thereof, or the lack of perfection or continuing perfection or failure of priority of any security for the Guaranteed Obligations or any part thereof;

(b) the absence of (i) any attempt to collect any Guaranteed Obligation or any part thereof from Borrower or any other Guarantor or other action to enforce the same or (ii) any action to enforce any Loan Document or any Lien thereunder;

(c) the failure by any Person to take any steps to perfect and maintain any Lien on, or to preserve any rights with respect to, any Collateral;

(d) any workout, insolvency, bankruptcy proceeding, reorganization, arrangement, liquidation or dissolution by or against Borrower, any other Guarantor or any of Borrower's other Subsidiaries or any procedure, agreement, order, stipulation, election, action or omission thereunder, including any discharge or disallowance of, or bar or stay against collecting, any Guaranteed Obligation (or any interest thereon) in or as a result of any such proceeding;

(e) any foreclosure, whether or not through judicial sale, and any other sale or other disposition of any Collateral or any election following the occurrence of an Event of Default and during the continuance thereof by the Collateral Agent, on behalf of Lenders and any other Secured Party, to proceed separately against any Collateral in accordance with the Collateral Agent's rights and the rights of any Lender or other Secured Party under any applicable Requirements of Law; or

(f) any other defense, setoff, counterclaim or any other circumstance that might otherwise constitute a legal or equitable discharge of Borrower, any other Guarantor or any other Subsidiary of Borrower, in each case other than the indefeasible payment in full of the Guaranteed Obligations (other than inchoate indemnity obligations).

Section 2.5. Waivers. To the fullest extent permitted by Requirements of Law, each Guarantor hereby unconditionally and irrevocably waives and agrees not to assert any claim, defense, setoff or counterclaim based on diligence, promptness, presentment, requirements for any demand or notice hereunder, including any of the following: (a) any demand for payment or performance and protest and notice of protest; (b) any notice of acceptance; (c) any presentment, demand, protest or further notice or other requirements of any kind with respect to any Guaranteed Obligation (including any accrued but unpaid interest thereon) becoming immediately due and payable; and (d) any other notice in respect of any Guaranteed Obligation or any part thereof, and any defense arising by reason of any disability or other defense of Borrower or any other Guarantor. Until the indefeasible payment in full of the Guaranteed Obligations (other than inchoate indemnity obligations), each Guarantor further unconditionally and irrevocably agrees not to (x) enforce or otherwise exercise any right of subrogation or any right of reimbursement or contribution or similar right against Borrower or any other Guarantor by reason of any Loan Document or any payment made thereunder or (y) assert any claim, defense, setoff or counterclaim it may have against any other Credit Party or set off any of its obligations to such other Credit Party against obligations of such Credit Party to such Guarantor. No obligation of any Guarantor hereunder shall be discharged other than by complete performance.

Section 2.6. Reliance. Each Guarantor hereby assumes responsibility for keeping itself informed of the financial condition of Borrower, each other Guarantor and any other guarantor, maker or endorser of any Guaranteed Obligation or any part thereof, and of all other circumstances bearing upon the risk of nonpayment of any Guaranteed Obligation or any part thereof that reasonable and diligent inquiry would reveal, and each Guarantor hereby agrees that neither the Collateral Agent nor any Lender or other Secured Party shall have any duty to advise any Guarantor of information known to it regarding such condition or any such circumstances. In the event the Collateral Agent, in its sole discretion, undertakes at any time or from time to time to provide any such information to any Guarantor, such Person shall be under no obligation to (a) undertake any investigation not a part of its regular business routine, (b) disclose any information that any Lender or other Secured Party, pursuant to accepted or reasonable commercial finance or banking practices, wishes to maintain confidential or (c) make any future disclosures of such information or any other information to any Guarantor.

Section 2.7. Contribution. To the extent that any Guarantor shall be required hereunder to pay any portion of any Guaranteed Obligation exceeding the greater of (a) the amount of the value actually received by such Guarantor and its Subsidiaries from the Term Loans and other Obligations and (b) the amount such Guarantor would otherwise have paid if such Guarantor had paid the aggregate amount of the Guaranteed Obligations (excluding the amount thereof repaid by Borrower) in the same proportion as such Guarantor's net worth on the date enforcement is sought hereunder bears to the aggregate net worth of all Guarantors on such date, then such Guarantor shall be reimbursed by such other Guarantors for the amount of such excess, *pro rata*, based on the respective net worth of such other Guarantors on such date.

ARTICLE III

GRANT OF SECURITY INTEREST

Section 3.1. Collateral. For the purposes of this Agreement, the following tangible and intangible assets and property now owned or at any time hereafter acquired, developed or created by a Grantor or in which a Grantor now has or at any time in the future may acquire any right, title or interest, in each case, wherever located, is collectively referred to as the "Collateral":

(a) all accounts;

(b) all as-extracted collateral;

(c) all chattel paper, including electronic chattel paper or tangible chattel paper;

(d) all checks;

(e) all deposit accounts;

(f) all documents;

(g) all encumbrances;

(h) all equipment;

(i) all fixtures;

(j) all general intangibles (including all agreements of any kind);

(k) all goods;

(l) all Intellectual Property and IP Licenses (including any IP Licenses under the Current Company IP Agreements to which a Grantor is a party and the rights of such Grantor thereunder, and all of a Grantor's right, title and interest in, to and under any Internet Domain Names and Software);

(m) all of a Grantor's right, title and interest in, to and under any NDA relating to the commercialization, marketing, offer for sale, distribution or sale of any Product in the Territory;

(n) all instruments (including all promissory notes);

(o) all inventory;

(p) all investment property (including Pledged Collateral, Pledged Investment Property, Equity Interests, securities, securities accounts and security entitlements with respect thereto and financial assets carried therein, and all commodity accounts and commodity contracts);

(q) all money;

(r) all letters of credit, letter-of-credit rights and supporting obligations;

(s) the commercial tort claims with a predicted value of $500,000 or more (as reasonably determined by a Responsible Officer of Borrower in good faith and based upon reasonable assumptions) described on Schedule 4 of the Security Disclosure Letter;

(t) all books, records, ledger cards, files, correspondence, customer lists, blueprints, technical specifications, manuals, computer software, computer printouts, tapes, disks and other electronic storage media and related data processing software and similar items that at any time pertain to or evidence or contain information relating to any of the other property described in this Section 3.1;

(u) all property of such Grantor held by the Collateral Agent for the benefit of Lenders and any other Secured Party, including all property of every description, in the custody of or in transit to the Collateral Agent for the benefit of Lenders and any other Secured Party for any purpose, including safekeeping, collection or pledge, for the account of such Grantor or as to which such Grantor may have any right or power, including cash;

(v) all proceeds, products, accessions, rents and profits of or in respect of any of the foregoing;

(w) to the extent not otherwise included, all personal property of such Grantor, whether tangible or intangible and wherever located, and all proceeds, products, accessions, rents, issues and profits of any and all of the foregoing and all collateral security, supporting obligations and guarantees given by any Person with respect to any of the foregoing; and

(x) to the extent not otherwise included, all other properties or assets of whatever kind and nature subject or purported to be subject from time to time to a Lien under any Collateral Document;

excluding, however, all Excluded Property.

Section 3.2. Grant of Security Interest in Collateral. Without limiting any other security interest granted to the Collateral Agent, in favor of and for the benefit of Lenders and the other Secured Parties, each Grantor, as collateral security for the prompt and complete payment and performance when due (whether at stated maturity, by acceleration or otherwise) of the Obligations of such Grantor (the "Secured Obligations"), hereby pledges, hypothecates and grants to the Collateral Agent, in favor and for the benefit of Lenders and the other Secured Parties, to secure the payment and performance in full of all of the Obligations for the benefit of Lenders and the other Secured Parties, a first priority Lien (subject only to Permitted Liens) on and continuing security interest in, all of its right, title and interest in, to and under the Collateral of such Grantor, wherever located, whether now owned or hereafter acquired or arising; provided, however, notwithstanding the foregoing, no Lien or security interest is hereby granted on, and "Collateral" shall not include, any Excluded Property; provided, further, that if and when any property or asset shall cease to be Excluded Property, a first priority Lien (subject only to Permitted Liens) on and security interest in such property or asset shall be deemed granted therein and, therefore, "Collateral" shall then include any such property or asset.

ARTICLE IV

REPRESENTATIONS AND WARRANTIES

To induce the Collateral Agent and Lenders to enter into the Loan Documents, each Grantor, jointly and severally with each other Grantor, represents and warrants each of the following to the Collateral Agent, each Lender and the other Secured Parties:

Section 4.1. Title; No Other Liens. Except for the Lien granted to the Collateral Agent for the benefit of Lenders and the other Secured Parties pursuant to this Agreement and any other Permitted Liens under any Loan Document (including Section 4.2 hereof), such Grantor owns or otherwise has the rights it purports to have in each item of the Collateral, free and clear of any and all Liens or claims of others. Such Grantor (a) is the record and beneficial owner of the Collateral pledged by it hereunder constituting instruments or certificates and (b) except for Permitted Subsidiary Distribution Restrictions, has rights in or the power to transfer each other item of Collateral in which a Lien is granted by it hereunder, free and clear of any other Lien other than any Permitted Liens.

Section 4.2. Perfection and Priority. Other than in respect of money and other Collateral subject to Section 9-311(a)(1) of the Code, the security interest granted to the Collateral Agent pursuant to this Agreement constitutes a valid and continuing first priority perfected security interest (subject, in the case of priority only, to Permitted Liens that are expressly permitted (if at all) by the terms of the Loan Agreement or this Agreement to have superior priority to the Lien and security interest granted to the Collateral Agent for the benefit of Lenders and the other Secured Parties) in favor of and for the benefit of Lenders and the other Secured Parties in all Collateral, subject, for the following Collateral, to the occurrence of the following: (a) in the case of all Collateral in which a security interest may be perfected by filing a financing statement under the Code, the completion of the filings and other actions specified on Schedule 2 of the Security Disclosure Letter (which, in the case of all filings and other documents referred to on such schedule, have been duly authorized by the applicable Guarantor); (b) with respect to any deposit account over which a Control Agreement is required pursuant to Section 5.5 of the Loan Agreement, the execution of Control Agreements; (c) in the case of all United States Trademarks, Patents and Copyrights for which Code filings are insufficient to effectuate perfection, all appropriate filings having been made with the Applicable IP Office, as applicable; (d) in the case of all Pledged Certificated Stock, the delivery thereof to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of such Pledged Certificated Stock consisting of instruments and certificates, in each case, properly endorsed for transfer to the Collateral Agent or in blank; (e) in the case of all Pledged Uncertificated Stock, the delivery to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of an executed uncertificated stock control agreement among the issuer, the registered owner and the Collateral Agent in the form attached as Annex 4 hereto; and (f) in the case of all other instruments that are not Pledged Stock, if any, the delivery thereof to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, of such instruments. Such Lien on and security interest in Pledged Stock shall be prior to all other Liens on such Collateral, subject to Permitted Liens having priority over the Collateral Agent's Lien by operation of law or as and to the extent expressly permitted (if at all) by any Loan Document. Except to the extent expressly not required pursuant to the terms of the Loan Agreement or this Agreement, all actions by each Grantor necessary or desirable to protect and perfect the first priority Lien on and security interest in the Collateral granted hereunder have been duly taken.

Section 4.3. Pledged Stock.

(a) The Pledged Stock issued by any Subsidiary of any Grantor pledged by such Grantor hereunder (i) consist of the number and types of Equity Interests listed on Schedule 1 of the Security Disclosure Letter and constitutes that percentage of the issued and outstanding equity of all classes of each issuer thereof as set forth on Schedule 1 of the Security Disclosure Letter, (ii) has been duly authorized, validly issued and is fully paid and nonassessable (other than Pledged Stock in limited liability companies and partnerships), and (ii) constitutes the legal, valid and binding obligation of the obligor with respect thereto, enforceable in accordance with its terms. As of the date any Joinder Agreement or Pledge Amendment is delivered pursuant to Section 8.6, the Pledged Stock pledged by each applicable Grantor thereunder (x) is listed on the applicable schedule attached to such Joinder Agreement or Pledge Amendment, as applicable, and constitutes that percentage of the issued and outstanding equity of all classes of each issuer thereof as set forth on such schedule, (y) has been duly authorized, validly issued and is fully paid and non-assessable (other than Pledged Stock in limited liability companies and partnerships) and (z) constitutes the legal, valid and binding obligation of the obligor with respect thereto, enforceable in accordance with its terms.

(b) (i) All Pledged Certificated Stock has been delivered to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, in accordance with Section 5.2(a), and (ii) with respect to Pledged Uncertificated Stock, uncertificated stock control agreements in the form attached as Annex 4 hereto have been delivered to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, in accordance with Section 5.2(a).

(c) Upon the occurrence and during the continuance of an Event of Default, the Collateral Agent for the benefit of Lenders and the other Secured Parties shall be entitled to exercise all of the rights of the Grantor granting the security interest in any Pledged Stock, and a transferee or assignee of such Pledged Stock shall become a holder of such Pledged Stock to the same extent as such Grantor and, upon the transfer of the entire interest of such Grantor, such Grantor shall, by operation of law, cease to be a holder of such Pledged Stock.

ARTICLE V

COVENANTS

Each Grantor agrees with the Collateral Agent to the following, until the indefeasible payment in full of the Obligations (other than inchoate indemnity obligations) and unless the Collateral Agent, on behalf of Lenders and the other Secured Parties, otherwise consents in writing:

Section 5.1. Maintenance of Perfected Security Interest; Further Documentation and Consents.

(a) Subject to the occurrence of the actions described in Section 4.2, which each Grantor shall promptly undertake, and except to the extent perfection is either (i) mutually agreed between Borrower and the Collateral Agent not to be required under this Agreement or the other Loan Documents or (ii) mutually agreed between Borrower and the Collateral Agent to be effected by filings of financing statements or amendments thereto to be made by the Collateral Agent or any Lender or its Related Party pursuant to Section 7.2, such Grantor shall maintain the security interest created by this Agreement as a perfected security interest having at least the priority described in Section 4.2 and shall warrant and defend the Collateral covered by such security interest and such priority against the claims and demands of all Persons (other than Secured Parties).

(b) Such Grantor shall furnish to the Collateral Agent at any time and from time to time statements and schedules further identifying and describing the Collateral and such other documents in connection with the Collateral as the Collateral Agent may reasonably request in writing, all in reasonable detail and in form and substance reasonably satisfactory to the Collateral Agent.

(c) At any time and from time to time, upon the written request of the Collateral Agent, such Grantor shall, for the purpose of obtaining or preserving the full benefits of this Agreement and the other Collateral Documents and of the rights and powers herein and therein granted, (i) promptly and duly execute and deliver, and have recorded, such further documents, including an authorization to file (or, as applicable, the filing) of any financing statement or amendment under the Code (or other filings under similar Requirements of Law) in effect in any jurisdiction with respect to the security interest created hereby and (ii) take such further action as the Collateral Agent may reasonably request in writing that is consistent with the requirements hereof and of the other Loan Documents, including executing and delivering any Control Agreements required by Section 5.5 of the Loan Agreement with respect to the Collateral Accounts.

Section 5.2. Pledged Collateral.

(a) Delivery of Pledged Collateral. Such Grantor shall, promptly after acquiring any Pledged Collateral not owned on the Tranche A Closing Date, (i) deliver to the Collateral Agent, in suitable form for transfer and in form and substance reasonably satisfactory to the Collateral Agent, (A) all such Pledged Stock that is Pledged Certificated Stock, (B) all Pledged Debt Instruments and (C) all certificates and instruments evidencing Pledged Investment Property, (ii) subject all Collateral Accounts required to be subject to a Control Agreement pursuant to the Loan Agreement to a Control Agreement, and (iii) cause the issuer of any such Pledged Stock that is Pledged Uncertificated Stock to execute an uncertificated stock control agreement in the form attached hereto as Annex 4, pursuant to which, *inter alia*, such issuer agrees to comply with the Collateral Agent's instructions with respect to such Pledged Uncertificated Stock without further consent by such Grantor, and, for the avoidance of doubt, if any such Pledged Uncertificated Stock becomes certificated, promptly (but in any event within thirty (30) days thereof) deliver to the Collateral Agent, in suitable form for transfer and in form and substance reasonably satisfactory to the Collateral Agent, all such certificates, instruments or other similar documents (as defined in the Code).

(b) Event of Default. During the continuance of any Event of Default and in connection with the exercise of rights or remedies hereunder or under any other Loan Document, the Collateral Agent shall have the right, at any time in its discretion and without prior notice to Grantor, to (i) transfer to or to register in its name or in the name of its nominees any Pledged Stock and (ii) exchange any certificate or instrument representing or evidencing any Pledged Stock for certificates or instruments of smaller or larger denominations; provided, that the Collateral Agent shall give written notice thereof to Grantor promptly following the occurrence (and, in any event, within two (2) Business Days of such occurrence) of any such transfer, registration or exchange; provided, further, that the failure of the Collateral Agent to deliver such notice shall not limit, affect or diminish any right of the Collateral Agent or the Lenders hereunder.

(c) Cash Distributions with respect to Pledged Collateral and Pledged Investment Property. Except as provided in Article VI and subject to any limitations set forth in the Loan Agreement, such Grantor shall be entitled to receive all cash distributions paid in respect of the Pledged Collateral and the Pledged Investment Property.

(d) Voting Rights. Except as provided in Article VI, such Grantor shall be entitled to exercise all voting, consent and corporate, partnership, limited liability company and similar rights with respect to the Pledged Collateral and Pledged Investment Property; provided, however, that no vote shall be cast, consent, waiver or ratification given or right exercised (or failed to be exercised) or other action taken (or failed to be taken) by such Grantor in any manner that would reasonably be expected to (i) violate or be inconsistent with any of the terms of this Agreement or any other Loan Document or (ii) have the effect of materially impairing such Collateral or the position or interests of the Secured Parties.

Section 5.3. Intellectual Property. Such Grantor shall, promptly (and in no event later than fifteen (15) days) after delivery of financial statements pursuant to Section 5.2(a) of the Loan Agreement), execute and deliver to Lender in form and substance reasonably acceptable to Lender and suitable for filing in the Applicable IP Office the short-form intellectual property security agreements in the form attached hereto as Annex 3 for all Collateral consisting of any newly-acquired Copyrights, Trademarks or Patents (as applicable) of such Grantor registered in the Applicable IP Office during the applicable reporting period.

ARTICLE VI

REMEDIAL PROVISIONS

Section 6.1. Code and Other Remedies.

(a) Code Remedies. During the continuance of an Event of Default, the Collateral Agent, on behalf of Lenders and the other Secured Parties, may exercise, in addition to all other rights and remedies granted to it in this Agreement, any IP Agreement, any other Loan Document or in any other instrument or agreement securing, evidencing or relating to any Secured Obligation, all rights, powers and remedies of a secured party under the Code or any other Requirements of Law or in equity.

(b) Disposition of Collateral. During the continuance of an Event of Default, without limiting the generality of the foregoing, the Collateral Agent may (personally or through its agents or attorneys), without demand of performance or other demand, presentment, protest, advertisement or notice of any kind (except any notice required by Requirements of Law referred to below) to or upon any Grantor or any other Person (all and each of which demands, defenses, advertisements and notices are hereby waived): (i) enter upon the premises where any Collateral is located, without any obligation to pay rent, through self-help, without judicial process, without first obtaining a final judgment or giving Grantor or any other Person notice or opportunity for a hearing on the Collateral Agent's or any Lender's claim or action; (ii) collect, receive, appropriate and realize upon any Collateral; (iii) store, process, repair or recondition the Collateral or otherwise prepare any Collateral for disposition in any manner to the extent the Collateral Agent deems appropriate; and (iv) sell, assign, license out, convey, transfer, grant option or options to purchase or license and deliver any Collateral (or enter into contractual obligations to do any of the foregoing), in one or more parcels at public or private sale or sales, at any exchange, broker's board or office of the Collateral Agent or any Lender or other Secured Party or elsewhere upon such terms and conditions as it may deem advisable and at such prices as it may deem best, for cash or on credit or for future delivery without assumption of any credit risk. The Collateral Agent, on behalf of Lenders and the other Secured Parties, shall have the right, upon any such public sale or sales and, to the extent permitted by the Code and other Requirements of Law, upon any such private sale or sales, to purchase or license the whole or any part of the Collateral so sold or licensed, free of any right or equity of redemption of any Grantor, which right or equity is hereby waived and released. The Collateral Agent, as representative of all Lenders and other Secured Parties, shall be entitled, for the purpose of bidding and making settlement or payment of the purchase price for all or any portion of the Collateral sold at any such sale made in accordance with the Code, to use and apply any of the Secured Obligations as a credit on account of the purchase price for any Collateral payable by the Collateral Agent on behalf of Lenders and the other Secured Parties, at such sale. If the Collateral Agent on behalf of any Lender sells any of the Collateral upon credit, Grantor will be credited only with payments actually made by purchaser and received by such Lender and applied to indebtedness of the purchaser. In the event the purchaser fails to pay for the Collateral, the Collateral Agent may resell the Collateral and Grantor shall be credited with proceeds of the sale. Neither the Collateral Agent nor any Lender shall have an obligation to marshal any of the Collateral.

(c) Management of the Collateral. Each Grantor further agrees, that, during the continuance of any Event of Default, (i) at the Collateral Agent's request, it shall assemble the Collateral and make it available to the Collateral Agent at places that the Collateral Agent shall reasonably select, whether at such Grantor's premises or elsewhere, (ii) without limiting the foregoing, the Collateral Agent also has the right to require that such Grantor store and keep any Collateral pending further action by the Collateral Agent and, while any such Collateral is so stored or kept, provide such guards and maintenance services as shall be necessary to protect the same and to preserve and maintain such Collateral in good condition, normal wear and tear excepted, (iii) until the Collateral Agent is able to sell, assign, license out, convey or transfer any Collateral, the Collateral Agent shall have the right to hold or use such Collateral to the extent that it deems appropriate for the purpose of preserving the Collateral or its value or for any other purpose

deemed appropriate by the Collateral Agent and (iv) the Collateral Agent may, if it so elects, seek the appointment of a receiver or keeper to take possession of any Collateral and to enforce any of the Collateral Agent's or any Lender's remedies, with respect to such appointment without prior notice or hearing as to such appointment. The Collateral Agent shall not have any obligation to any Grantor to maintain or preserve the rights of any Grantor as against other Persons with respect to any Collateral while such Collateral is in the possession of the Collateral Agent.

(d) Application of Proceeds. The Collateral Agent shall apply the cash proceeds received by it in respect of any sale of, any collection from, or other realization upon all or any part of the Collateral, after deducting all reasonable costs and expenses of every kind incurred in connection therewith or incidental to the care or safekeeping of any Collateral or in any way relating to the Collateral or the rights of Lenders and the other Secured Parties, including reasonable and documented out-of-pocket attorneys' fees and disbursements, to the payment in whole or in part of the Secured Obligations, as set forth in the Loan Agreement, and only after such application and after the payment by the Collateral Agent or Lenders of any other amount required by any Requirements of Law, need the Collateral Agent or any Lender account for the surplus, if any, to any Grantor.

(e) Direct Obligation. Neither the Collateral Agent nor any Lender or other Secured Party shall be required to make any demand upon, or pursue or exhaust any right or remedy against, any Grantor or any other Person with respect to the payment of the Obligations or to pursue or exhaust any right or remedy with respect to any Collateral therefor or any direct or indirect guaranty thereof. All of the rights and remedies of the Collateral Agent and Lenders and any other Secured Party shall be cumulative, may be exercised individually or concurrently and not exclusive of any other rights or remedies provided by any Requirements of Law. To the extent it may lawfully do so, each Grantor absolutely and irrevocably waives and relinquishes the benefit and advantage of, and covenants not to assert against the Collateral Agent, Lenders or any other Secured Party, any valuation, stay, appraisement, extension, redemption or similar laws and any and all rights or defenses it may have as a surety, now or hereafter existing, arising out of the exercise by any of them of any rights or remedies hereunder. If any notice of a proposed sale or other disposition of any Collateral shall be required by Requirements of Law, such notice shall be deemed reasonable and proper if given at least ten (10) days before such sale or other disposition.

(f) Commercially Reasonable. To the extent that applicable Requirements of Law impose duties on the Collateral Agent or any Lender or other Secured Party to exercise remedies in a commercially reasonable manner, each Grantor acknowledges and agrees that it is not commercially unreasonable for the Collateral Agent or any Lender to do any of the following:

(i) fail to incur significant costs, expenses or other liabilities reasonably deemed as such by the Collateral Agent or such Lender to prepare any Collateral for disposition or otherwise to complete raw material or work in process into finished goods or other finished products for disposition;

(ii) fail to obtain permits, licenses or other consents for access to any Collateral to sell or license or for the collection or sale or licensing of any Collateral, or, if not required by other Requirements of Law, fail to obtain permits, licenses or other consents for the collection or disposition of any Collateral;

(iii) fail to exercise remedies against account debtors or other Persons obligated on any Collateral or to remove Liens on any Collateral or to remove any adverse claims against any Collateral;

(iv) advertise dispositions of any Collateral through publications or media of general circulation, whether or not such Collateral is of a specialized nature, or to contact other Persons, whether or not in the same business as any Grantor, for expressions of interest in acquiring any such Collateral;

(v) exercise collection remedies against account debtors and other Persons obligated on any Collateral, directly or through the use of collection agencies or other collection specialists, hire one or more professional auctioneers to assist in the disposition of any Collateral, whether or not such Collateral is of a specialized nature, or, to the extent deemed appropriate by the Collateral Agent or such Lender, obtain the services of other brokers, investment bankers, consultants and other professionals to assist the Collateral Agent or such Lender in the collection or disposition of any Collateral, or utilize Internet sites that provide for the auction of assets of the types included in the Collateral or that have the reasonable capacity of doing so, or that match buyers and sellers of assets to dispose of any Collateral;

(vi) dispose of assets in wholesale rather than retail markets;

(vii) disclaim warranties, such as title, merchantability, possession, non-infringement or quiet enjoyment; or

(viii) purchase insurance or credit enhancements to insure the Collateral Agent or any Lender or other Secured Party against risks of loss, collection or disposition of any Collateral or to provide to the Collateral Agent and Lenders a guaranteed return from the collection or disposition of any Collateral.

Each Grantor acknowledges that the purpose of this Section 6.1 is to provide a non-exhaustive list of actions or omissions that are commercially reasonable when exercising remedies against any Collateral and that other actions or omissions by the Collateral Agent, Lenders or any other Secured Party shall not be deemed commercially unreasonable solely on account of not being indicated in this Section 6.1. Without limitation upon the foregoing, nothing contained in this Section 6.1 shall be construed to grant any rights to any Grantor or to impose any duties on the Collateral Agent or any Lender or other Secured Party that would not have been granted or imposed by this Agreement or by applicable Requirements of Law in the absence of this Section 6.1.

(g) IP Licenses. To the extent permitted, and only for the purpose of enabling the Collateral Agent to exercise rights and remedies under this Section 6.1 (including in order to take possession of, collect, receive, assemble, process, appropriate, remove, realize upon, sell, assign, license out, convey, transfer or grant options to purchase any Collateral) at such time as the Collateral Agent on behalf of Lenders and the other Secured Parties shall be lawfully entitled to exercise such rights and remedies, each Grantor hereby grants to the Collateral Agent (i) an irrevocable, nonexclusive, assignable, worldwide license (exercisable without payment of royalty or other compensation to such Grantor), including the right to sublicense, use and practice any and all Intellectual Property now owned or held or hereafter acquired or held by such Grantor and

access to all media in which any of the licensed items may be recorded or stored and to all Software and programs used for the compilation or printout thereof and (ii) an irrevocable license (without payment of rent or other compensation to such Grantor) to use, operate and occupy all real property owned, operated, leased, subleased or otherwise occupied by such Grantor.

Section 6.2. Accounts and Payments in Respect of General Intangibles.

(a) In addition to, and not in substitution for, any similar requirement in the Loan Agreement, if required by the Collateral Agent at any time during the continuance of an Event of Default, any payment of accounts or payment in respect of general intangibles relating to the Collateral, when collected by any Grantor, shall be promptly (and, in any event, within two (2) Business Days of such collection) deposited by such Grantor in the exact form received, duly indorsed by such Grantor to the Collateral Agent for the benefit of Lenders and the other Secured Parties, in a Collateral Account, subject to withdrawal by the Collateral Agent as provided in Section 6.4. Until so turned over, such payment shall be held by such Grantor in trust for the Collateral Agent for the benefit of Lenders and the other Secured Parties, segregated from other funds of such Grantor. Each such deposit of proceeds of accounts and payments in respect of general intangibles relating to the Collateral shall, upon the Collateral Agent's request, be accompanied by a report identifying in reasonable detail the nature and source of the payments included in the deposit.

(b) At any time during the continuance of an Event of Default:

(i) each Grantor shall, upon the Collateral Agent's request, assemble and hold for the benefit of Lenders and the other Secured Parties all original and other documents evidencing, and relating to, the contractual obligations and transactions that gave rise to any account or any payment in respect of general intangibles, including all IP Licenses, original orders, invoices and shipping receipts and notify account debtors that the accounts or general intangibles have been collaterally assigned to the Collateral Agent for the benefit of Lenders and the other Secured Parties and that payments in respect thereof shall be made directly to the Collateral Agent for the benefit of Lenders and the other Secured Parties or to any Lender on behalf of itself and the other Secured Parties, as the Collateral Agent shall direct; and

(ii) each Grantor shall take all actions, deliver all documents and provide all information necessary or reasonably requested by the Collateral Agent to ensure any Internet Domain Name is registered.

(c) Anything herein to the contrary notwithstanding, each Grantor shall remain liable under each account and each payment in respect of general intangibles included in the Collateral to observe and perform all the conditions and obligations to be observed and performed by it thereunder, all in accordance with the terms of any agreement giving rise thereto. Neither the Collateral Agent nor any Lender or other Secured Party shall have any obligation or liability under any agreement giving rise to an account or a payment in respect of a general intangible included in the Collateral by reason of or arising out of any Loan Document or the receipt by the Collateral Agent or any Lender or other Secured Party of any payment relating thereto, nor shall the Collateral Agent nor any Lender or other Secured Party be obligated in any manner to perform any obligation of any Grantor under or pursuant to any agreement giving rise to an account or a

payment in respect of a general intangible included in the Collateral, to make any payment, to make any inquiry as to the nature or the sufficiency of any payment received by it or as to the sufficiency of any performance by any party thereunder, to present or file any claim, to take any action to enforce any performance or to collect the payment of any amounts that may have been assigned to it or to which it may be entitled at any time or times.

Section 6.3. Pledged Collateral.

(a) Voting Rights. Upon two (2) Business Days' prior written notice to Grantor, during the continuance of an Event of Default, all rights of each Grantor to exercise or refrain from exercising the voting and other consensual rights which it would otherwise be entitled to exercise pursuant hereto shall cease and all such rights shall thereupon become vested in the Collateral Agent or a nominee on behalf of Lenders or the other Secured Parties, who shall thereupon have the sole right to exercise such voting and other consensual rights, including the right to exercise (i) any voting, consent, corporate and other right pertaining to the Pledged Collateral at any meeting of shareholders, partners or members, as the case may be, of the relevant issuer or issuers of Pledged Collateral or otherwise, and (ii) any right of conversion, exchange and subscription and any other right, privilege or option pertaining to the Pledged Collateral as if it were the absolute owner thereof (including the right to exchange at its discretion any Pledged Collateral upon the merger, amalgamation, consolidation, reorganization, recapitalization or other fundamental change in the corporate or equivalent structure of any issuer of Pledged Collateral, the right to deposit and deliver any Pledged Collateral with any committee, depositary, transfer agent, registrar or other designated agency upon such terms and conditions as the Collateral Agent (or such nominee) on behalf of Lenders or the other Secured Parties may determine), all without liability except to account for property actually received by it; provided, however, that the Collateral Agent (or such nominee) shall have no duty to any Grantor to exercise any such right, privilege or option and shall not be responsible for any failure to do so or delay in so doing; provided, further, that the failure of the Collateral Agent (or such nominee) to deliver such notice shall not limit, affect or diminish any right of the Collateral Agent or the Lenders hereunder.

(b) Proxies. Upon two (2) Business Days' prior written notice to Grantor, during the continuance of an Event of Default, in order to permit the Collateral Agent on behalf of Lenders and the other Secured Parties to exercise the voting and other consensual rights that it may be entitled to exercise pursuant hereto and to receive all dividends and other distributions that it may be entitled to receive hereunder, (i) each Grantor shall promptly execute and deliver (or cause to be executed and delivered) to the Collateral Agent all such proxies, dividend payment orders and other instruments as the Collateral Agent may from time to time reasonably request and (ii) without limiting the effect of clause (i) above, such Grantor hereby grants to the Collateral Agent for the benefit of Lenders and the other Secured Parties an irrevocable proxy to vote all or any part of the Pledged Collateral and to exercise all other rights, powers, privileges and remedies to which a holder of the Pledged Collateral would be entitled (including giving or withholding written consents of shareholders, partners or members, as the case may be, calling special meetings of shareholders, partners or members, as the case may be, and voting at such meetings), which proxy shall be effective, automatically and without the necessity of any action (including any transfer of any Pledged Collateral on the record books of the issuer thereof) by any other Person (including the issuer of such Pledged Collateral or any officer or agent thereof) during the continuance of an Event of Default and which proxy shall only terminate upon (A) the cure of any and all Events of Default or (B) the indefeasible payment in full of the Secured Obligations (other than contingent indemnification obligations to the extent no claim giving rise thereto has been asserted); provided, however, that the failure of the Collateral Agent to deliver such notice shall not limit, affect or diminish any right of the Collateral Agent or the Lenders hereunder.

(c) Authorization of Issuers. Each Grantor hereby expressly and irrevocably authorizes and instructs, without any further instructions from such Grantor, each issuer of any Pledged Collateral pledged hereunder by such Grantor to, and each Grantor that is an issuer of Pledged Collateral so pledged hereunder hereby agrees to (i) comply with any instruction received by it from the Collateral Agent in writing that states that an Event of Default is continuing in accordance with the terms of this Agreement and each Grantor agrees that such issuer shall be fully protected from liabilities to such Grantor in so complying, and (ii) during the continuance of such Event of Default, unless otherwise permitted hereby or by the Loan Agreement, pay any dividend or make any other payment with respect to the Pledged Collateral directly to the Collateral Agent for the benefit of Lenders and the other Secured Parties or to any Lender on behalf of itself and the other Secured Parties, as the Collateral Agent shall direct.

Section 6.4. Proceeds to be Turned over to and Held by Collateral Agent. Unless otherwise expressly provided in the Loan Agreement or this Agreement, during the continuance of an Event of Default and, upon written notice by the Collateral Agent to the relevant Grantor or Grantors, all proceeds of any Collateral received by any Grantor hereunder in cash or Cash Equivalents shall be held by such Grantor in trust for Lenders and the other Secured Parties, segregated from other funds of such Grantor, and shall, promptly upon receipt by any Grantor, be turned over to the Collateral Agent for the benefit of Lenders and the other Secured Parties in the exact form received (with any necessary endorsement). All such proceeds of Collateral and any other proceeds of any Collateral received by the Collateral Agent in cash or Cash Equivalents shall be held by the Collateral Agent for the benefit of itself and the other Secured Parties in a Collateral Account. All proceeds being held by the Collateral Agent in a Collateral Account (or by such Grantor in trust for Lenders and the other Secured Parties) shall continue to be held as collateral security for the Secured Obligations and shall not constitute payment thereof until applied as provided in the Loan Agreement.

Section 6.5. Sale of Pledged Collateral.

(a) Each Grantor recognizes that the Collateral Agent may be unable to effect a public sale of any Pledged Collateral by reason of certain prohibitions contained in the Securities Act and applicable state or foreign securities laws or otherwise or may determine that a public sale is impracticable, not desirable or not commercially reasonable and, accordingly, may resort to one or more private sales thereof to a restricted group of purchasers that shall be obliged to agree, among other things, to acquire such securities for their own account for investment and not with a view to the distribution or resale thereof. Each Grantor acknowledges and agrees that any such private sale may result in prices and other terms less favorable than if such sale were a public sale and, notwithstanding such circumstances, agrees that any such private sale shall be deemed to have been made in a commercially reasonable manner. The Collateral Agent shall be under no obligation to delay a sale of any Pledged Collateral for the period of time necessary to permit the issuer thereof to register such securities for public sale under the Securities Act or under applicable state securities laws even if such issuer would agree to do so.

(b) Each Grantor agrees to use commercially reasonable efforts to do or cause to be done all such other acts as may be reasonably necessary to make such sale or sales of any portion of the Pledged Collateral pursuant to Section 6.1 and this Section 6.5 valid and binding and in compliance with all applicable Requirements of Law. Each Grantor further agrees that a breach of any covenant contained herein will cause irreparable injury to the Collateral Agent, Lenders and the other Secured Parties, that the Collateral Agent, Lenders and the other Secured Parties have no adequate remedy at law in respect of such breach and, as a consequence, that each and every covenant contained herein shall be specifically enforceable against such Grantor, and such Grantor hereby waives and agrees not to assert any defense against an action for specific performance of such covenants except for a defense that no Event of Default has occurred and is continuing under the Loan Agreement or a defense of indefeasible payment in full of the Guaranteed Obligations (other than inchoate indemnity obligations). Each Grantor waives any and all rights of contribution or subrogation upon the sale or disposition of all or any portion of the Pledged Collateral by the Collateral Agent on behalf of Lenders and the other Secured Parties.

Section 6.6. Deficiency. Each Grantor shall remain liable for any deficiency if the proceeds of any sale or other disposition of any Collateral are insufficient to pay the Secured Obligations and the reasonable and documented fees and disbursements of any attorney employed by the Collateral Agent or any Lender to collect such deficiency.

Section 6.7. Collateral Accounts. If any Event of Default shall have occurred and be continuing, the Collateral Agent may apply the balance from any Collateral Account of a Grantor or instruct the bank at which any Collateral Account is maintained to pay the balance of any Collateral Account to the Collateral Agent for the benefit of Lenders and the other Secured Parties or to any Lender on behalf of itself and the other Secured Parties, as the Collateral Agent shall direct, to be applied to the Secured Obligations in accordance with the terms hereof.

Section 6.8. Directions, Notices or Instructions. Neither the Collateral Agent nor any Lender or any Related Party thereof or any other Secured Party shall take any action under or issue any directions, notice or instructions pursuant to any Control Agreement or similar agreement unless an Event of Default has occurred and is continuing.

ARTICLE VII

ADDITIONAL RIGHTS OF COLLATERAL AGENT

Section 7.1. Collateral Agent's Appointment as Attorney-in-Fact.

(a) Each Grantor hereby irrevocably constitutes and appoints the Collateral Agent and any Related Party thereof, with full power of substitution, as its true and lawful attorney-in-fact with full irrevocable power and authority in the place and stead of such Grantor and in the name of such Grantor or in its own name, for the purpose of carrying out the terms of the Loan Documents, to take any appropriate action and to execute any document or instrument that may be necessary or desirable to accomplish the purposes of the Loan Documents, in each case during the continuance of an Event of Default, and, without limiting the generality of the foregoing, each Grantor hereby gives the Collateral Agent and its Related Party the power and right, on behalf of such Grantor, without notice to or assent by such Grantor, to do any of the following when an Event of Default shall be continuing:

(i) in the name of such Grantor, in its own name or otherwise, take possession of and indorse and collect any check, draft, note, acceptance or other instrument for the payment of moneys due under any account or general intangible or with respect to any other Collateral and file any claim or take any other action or proceeding in any court of law or equity or otherwise deemed appropriate by the Collateral Agent for the purpose of collecting any such moneys due under any account or general intangible or with respect to any other Collateral whenever payable;

(ii) in the case of any Intellectual Property (including any IP Ancillary Rights) or any IP Licenses included in the Collateral, execute, deliver and have recorded any document that the Collateral Agent may request to evidence, effect, publicize or record the Collateral Agent's security interest, in favor of and for the benefit of Lenders and the other Secured Parties, in such Intellectual Property or IP Licenses and the goodwill and general intangibles of such Grantor relating thereto or represented thereby and the Collateral Agent's (on behalf of Lenders and the other Secured Parties) rights and remedies with respect thereto;

(iii) pay or discharge taxes and Liens levied or placed on or threatened against any Collateral, effect any repair or obtain or pay any insurance called for by the terms of the Loan Agreement (including all or any part of the premiums therefor and the costs thereof);

(iv) execute, in connection with any sale provided for in Section 6.1 or 6.5, any document to effect or otherwise necessary or appropriate in relation to evidence the sale of any Collateral; or

(v) (A) direct any party liable for any payment under any Collateral to make payment of any moneys due or to become due thereunder directly to the Collateral Agent or as the Collateral Agent shall direct, (B) ask or demand for, and collect and receive payment of and receipt for, any moneys, claims and other amounts due or to become due at any time in respect of or arising out of any Collateral, (C) commence and prosecute any suit, action or proceeding at law or in equity in any court of competent jurisdiction to collect any Collateral and to enforce any other right in respect of any Collateral, (D) defend any actions, suits, proceedings, audits, claims, demands, orders or disputes brought against such Grantor with respect to any Collateral, (E) settle, compromise or adjust any such actions, suits, proceedings, audits, claims, demands, orders or disputes and, in connection therewith, give such discharges or releases as the Collateral Agent may deem appropriate, (F) assign or license any Intellectual Property included in the Collateral on such terms and conditions and in such manner as the Collateral Agent shall in its sole discretion determine, including the execution and filing of any document necessary to effectuate or record such assignment or license and (G) generally, sell, assign, license, convey, transfer or grant a Lien on, make any contractual obligation with respect to and otherwise deal with, any Collateral as fully and completely as though the Collateral Agent on behalf of Lenders and the other Secured Parties were the absolute owner thereof for all purposes and do, at the Collateral Agent's option, at any time or from time to time, all acts and things that the Collateral Agent deems necessary to protect, preserve or realize upon any Collateral and the Collateral Agent's, in favor of and for the benefit of Lenders and the other Secured Parties, security interests therein and to effect the intent of the Loan Documents, all as fully and effectively as such Grantor might do.

(vi) If any Grantor fails to perform or comply with any contractual obligation contained herein, the Collateral Agent, at its option, but without any obligation so to do, may perform or comply, or otherwise cause performance or compliance, with such contractual obligation.

(b) The reasonable and documented out-of-pocket expenses of the Collateral Agent and any Lender and other Secured Party incurred in connection with actions undertaken as provided in this Section 7.1, together with interest thereon at the Default Rate, from the date of payment by such Person to the date reimbursed by the relevant Grantor, shall be payable by such Grantor to such Person on demand.

(c) Each Grantor hereby ratifies all that said attorneys shall lawfully do or cause to be done by virtue of this Section 7.1. All powers, authorizations and agencies contained in this Agreement are coupled with an interest and are irrevocable until the indefeasible payment in full of the Secured Obligations (other than inchoate indemnity obligations), this Agreement is terminated and the security interests created hereby are released.

Section 7.2. Authorization to File Financing Statements. Each Grantor authorizes the Collateral Agent and its Related Party, at any time and from time to time, without notice to any Grantor, to file or record financing statements, amendments thereto, and other filing or recording documents or instruments with respect to any Collateral in such form, in such jurisdictions and in such offices as the Collateral Agent reasonably determines appropriate to perfect or protect the security interests of the Collateral Agent, in favor of and for the benefit of Lenders and the other Secured Parties, under this Agreement or any other Loan Document (and the Collateral Agent's and each Lender's and each other Secured Party's rights in respect thereof), and such financing statements and amendments may describe the Collateral covered thereby as "all assets of the debtor" or words of similar effect and may include a notice that any disposition of the Collateral, by any Grantor or other Person, shall be deemed to violate the rights of the Collateral Agent and Lenders and other Secured Parties under the Code to the extent not permitted under this Agreement or any other Loan Document. A photographic or other

reproduction of this Agreement shall be sufficient as a financing statement or other filing or recording document or instrument for filing or recording in any jurisdiction. Such Grantor also hereby ratifies its authorization for the Collateral Agent to have filed any initial financing statement or amendment thereto under the Code (or other similar laws) in effect in any jurisdiction if filed prior to the date hereof.

Section 7.3. Authority of Collateral Agent. Each Grantor acknowledges that, as between the Collateral Agent and the Grantors, the Collateral Agent shall be conclusively presumed to be acting as agent for each Lender and all of the other Secured Parties with full and valid authority so to act or refrain from acting, and no Grantor shall be under any obligation or entitlement to make any inquiry respecting such authority.

Section 7.4. Duty; Obligations and Liabilities.

(a) Duty of Collateral Agent. The Collateral Agent's sole duty with respect to the custody, safekeeping and physical preservation of the Collateral in its possession shall be to deal with it in the same manner as it deals with similar property for its own account. The powers conferred on the Collateral Agent hereunder are solely to protect each Lender's and the other Secured Parties' interest in the Collateral and shall not impose any duty upon the Collateral Agent to exercise any such powers. The Collateral Agent shall be accountable only for amounts that it receives as a result of the exercise of such powers, and neither it nor any of its Related Parties shall be responsible to any Grantor for any act or failure to act hereunder, except for its or their own gross negligence, bad faith or willful misconduct as finally determined by a court of competent jurisdiction. In addition, the Collateral Agent shall not be liable or responsible for any loss or damage to any Collateral, or for any diminution in the value thereof, by reason of the act or omission of any warehousemen, carrier, forwarding agency, consignee or other bailee if such Person has been selected by the Collateral Agent in good faith.

(b) Obligations and Liabilities with respect to Collateral. Neither the Collateral Agent nor Lenders or any other Secured Parties nor any of their respective Related Parties shall be liable for failure to demand, collect or realize upon any Collateral or for any delay in doing so or shall be under any obligation to sell or otherwise dispose of any Collateral upon the request of any Grantor or any other Person or to take any other action whatsoever with regard to any Collateral.

ARTICLE VIII

MISCELLANEOUS

Section 8.1. Reinstatement. Each Grantor agrees that, if any payment made by any Credit Party or other Person and applied to the Secured Obligations is at any time annulled, avoided, set aside, rescinded, invalidated, declared to be fraudulent or preferential or otherwise required to be refunded or repaid, or the proceeds of any Collateral are required to be returned by any Secured Party to such Credit Party, its estate, trustee, receiver or any other party, including any Grantor, under any bankruptcy law, state or federal law, common law or equitable cause, then, to the extent of such payment or repayment, any Lien or other Collateral securing such liability shall be and remain in full force and effect, as fully as if such payment had never been

made. If, prior to any of the foregoing, (a) any Lien or other Collateral securing such Grantor's liability hereunder shall have been released or terminated by virtue of the foregoing or (b) any provision of the Guaranty hereunder shall have been terminated, cancelled or surrendered, such Lien, other Collateral or provision shall be reinstated in full force and effect and such prior release, termination, cancellation or surrender shall not diminish, release, discharge, impair or otherwise affect the obligations of such Grantor in respect of any Lien or other Collateral securing such obligation or the amount of such payment.

Section 8.2. Release of Collateral and Guarantee Obligations.

(a) When all Obligations (other than inchoate indemnity obligations) have indefeasibly been paid in full, the Collateral shall be released from the Lien created hereby and this Agreement and all obligations (other than those expressly stated to survive such termination) of each Lender and any other Secured Party and each Guarantor and Grantor hereunder shall terminate, all without delivery of any instrument or performance of any act by any party (except as required hereunder), and all rights of the Collateral Agent, Lenders and any other Secured Parties to the Collateral shall revert to the Grantors.

(b) In connection with any termination or release pursuant to this Section 8.2, the Collateral Agent shall, and to the extent required, each Secured Party hereby authorizes the Collateral Agent to, promptly execute and deliver to any Grantor all instruments, documents and agreements which such Grantor shall reasonably request in writing to evidence and confirm such termination or release (including termination statements under the Code), and will duly assign, transfer and deliver to such Grantor (or its designee), such of the Collateral that may be in the possession of the Collateral Agent, all without further consent or joinder of the Collateral Agent or any Lender or other Secured Party.

(c) Any termination or release pursuant to this Section 8.2 is subject to reinstatement as provided in Section 8.1.

(d) Upon the release of the Liens on any Collateral or of a Grantor from all of its obligations as a Credit Party under the Loan Agreement and as a Grantor hereunder, any representation, warranty or covenant contained in any Loan Document relating to any such Collateral or such Grantor, as applicable, shall no longer be deemed to be made.

(e) Without limiting the generality of Section 2.4 of the Loan Agreement, Borrower agrees to pay all reasonable and documented out-of-pocket expenses incurred by the Collateral Agent and each Lender and other Secured Party in connection with the taking of any actions pursuant to or as otherwise contemplated by this Section 8.2.

Section 8.3. Independent Obligations. The obligations of each Grantor hereunder are independent of and separate from the Secured Obligations and the Guaranteed Obligations. Upon any Event of Default and during the continuance thereof, the Collateral Agent for the benefit of Lenders and the other Secured Parties may, at its sole election, proceed directly and at once, without notice, against any Grantor and any Collateral to collect and recover the full amount of any Secured Obligation or Guaranteed Obligation then due, without first

proceeding against any other Grantor, any other Credit Party or any other Collateral and without first joining any other Grantor or any other Credit Party in any proceeding.

Section 8.4. No Waiver by Course of Conduct. Neither the Collateral Agent nor any Secured Party shall by any act (except by a written instrument pursuant to Section 8.5), delay, indulgence, omission or otherwise be deemed to have waived any right or remedy hereunder or to have acquiesced in any Default or Event of Default. No failure to exercise, nor any delay in exercising, on the part of the Collateral Agent or any Secured Party, any right, power or privilege hereunder shall operate as a waiver thereof. No single or partial exercise of any right, power or privilege hereunder shall preclude any other or further exercise thereof or the exercise of any other right, power or privilege. A waiver by the Collateral Agent or any Secured Party of any right or remedy hereunder on any one occasion shall not be construed as a bar to any right or remedy that the Collateral Agent or any Secured Party would otherwise have on any future occasion.

Section 8.5. Amendments in Writing. None of the terms or provisions of this Agreement may be waived, amended, supplemented or otherwise modified except in accordance with Section 11.5 of the Loan Agreement; provided, however, that annexes to this Agreement may be supplemented (but no existing provisions may be modified and no Collateral may be released) through Pledge Amendments and Joinder Agreements, in substantially the form of Annex 1 and Annex 2 attached hereto, respectively, in each case, duly executed by the Collateral Agent and each Grantor directly affected thereby.

Section 8.6. Additional Grantors and Guarantors; Additional Pledged Collateral.

(a) Joinder Agreements. If, at the option of Borrower or as required pursuant to Section 5.12 or Section 5.13 of the Loan Agreement, Borrower shall cause any Subsidiary (other than an Excluded Subsidiary) that is not a Grantor or Guarantor to become a Grantor and Guarantor hereunder, such Subsidiary shall execute and deliver to the Collateral Agent a Joinder Agreement substantially in the form of Annex 2 attached hereto and shall thereafter for all purposes be a party hereto and have the same rights, benefits and obligations as a Grantor party hereto on the Closing Date.

(b) Pledge Amendments. To the extent any Pledged Collateral has not been delivered as of the Tranche A Closing Date, such Grantor shall, promptly after such Pledged Collateral is acquired, deliver a pledge amendment duly executed by the Grantor in substantially the form of Annex 1 attached hereto (each, a "Pledge Amendment"). Such Grantor authorizes the Collateral Agent to attach each Pledge Amendment to this Agreement.

Section 8.7. Notices. All notices, requests and demands to or upon the Collateral Agent or any Grantor hereunder shall be effected in the manner provided for in Section 9 of the Loan Agreement; provided, however, that any such notice, request or demand to or upon any Grantor shall be addressed to Borrower's notice address set forth in Section 9 of the Loan Agreement.

Section 8.8. Successors and Assigns. This Agreement shall be binding upon the successors and assigns of each Grantor and shall inure to the benefit of the Collateral Agent and each Secured Party and their respective successors and assigns; provided, however, that no Grantor may assign, transfer or delegate any of its rights or obligations under this Agreement without the prior written consent of the Collateral Agent.

Section 8.9. Counterparts. This Agreement may be executed in any number of counterparts and by different parties in separate counterparts, each of which when so executed shall be deemed to be an original and all of which taken together shall constitute one and the same agreement. Signature pages may be detached from multiple separate counterparts and attached to a single counterpart. Delivery of an executed signature page of this Agreement by facsimile transmission or by electronic transmission shall be as effective as delivery of a manually executed counterpart hereof.

Section 8.10. Severability. Any provision of this Agreement being held illegal, invalid or unenforceable in any jurisdiction shall not affect any part of such provision not held illegal, invalid or unenforceable, any other provision of this Agreement or any part of such provision in any other jurisdiction.

Section 8.11. Governing Law. This Agreement and the rights and obligations of the parties hereto shall be governed by, and construed and interpreted in accordance with, the law of the State of New York without regard to any principle of conflicts of law that could require the application of the law of any other jurisdiction.

Section 8.12. Waiver of Jury Trial. TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, EACH PARTY HERETO HEREBY IRREVOCABLY WAIVES TRIAL BY JURY IN ANY SUIT, ACTION OR PROCEEDING WITH RESPECT TO, OR DIRECTLY OR INDIRECTLY ARISING OUT OF, UNDER OR IN CONNECTION WITH, THIS AGREEMENT, ANY OTHER LOAN DOCUMENT OR THE TRANSACTIONS CONTEMPLATED HEREIN AND THEREIN OR RELATED HERETO OR THERETO (WHETHER FOUNDED IN CONTRACT, TORT OR ANY OTHER THEORY). EACH PARTY HERETO (A) CERTIFIES THAT NO OTHER PARTY AND NO RELATED PARTY OF ANY OTHER PARTY HAS REPRESENTED, EXPRESSLY OR OTHERWISE, THAT SUCH OTHER PARTY WOULD NOT, IN THE EVENT OF LITIGATION, SEEK TO ENFORCE THE FOREGOING WAIVER, (B) ACKNOWLEDGES THAT IT AND THE OTHER PARTIES HERETO HAVE BEEN INDUCED TO ENTER INTO THIS AGREEMENT BY THE MUTUAL WAIVERS AND CERTIFICATIONS IN THIS SECTION 8.12 AND (C) HAS REVIEWED THIS WAIVER WITH ITS COUNSEL.

EACH GRANTOR AGREES TO BE BOUND BY THE PROVISIONS OF SECTION 10 OF THE LOAN AGREEMENT.

[Signature Pages Follow]

IN WITNESS WHEREOF, each of the undersigned has caused this Guaranty and Security Agreement to be duly executed and delivered as of the date first above written.

GLOBAL BLOOD THERAPEUTICS, INC.,
as Borrower and Grantor

By_____

Name:_____

Title:_____

ACCEPTED AND AGREED
as of the date first above written:

BIOPHARMA CREDIT PLC,
as Collateral Agent

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By _____
Name: Pedro Gonzalez de Cosio
Title: Managing Member

ANNEX 1
TO GUARANTY AND SECURITY AGREEMENT

FORM OF PLEDGE AMENDMENT

This Pledge Amendment, dated as of _____, 20__, is delivered pursuant to Section 8.6 of the Guaranty and Security Agreement, dated as of [_____], 2019, by GLOBAL BLOOD THERAPEUTICS, INC., as Borrower, [_____], a [_____], as a Grantor, the undersigned Grantor and the other Persons from time to time party thereto as Grantors in favor of BIOPHARMA CREDIT PLC, as Collateral Agent on behalf of Lenders and each of the other Secured Parties (as such agreement may be amended, restated, supplemented or otherwise modified from time to time, the "Guaranty and Security Agreement"). Capitalized terms used herein without definition are used as defined in the Guaranty and Security Agreement.

The undersigned hereby agrees that this Pledge Amendment may be attached to the Guaranty and Security Agreement and that the Pledged Collateral listed on Annex 1-A to this Pledge Amendment shall be and become part of the Collateral referred to in the Guaranty and Security Agreement and shall secure all Secured Obligations of the undersigned.

[GRANTOR]

By:_____
Name:
Title:

PLEDGED STOCK

ISSUER	CLASS	CERTIFICATE NO(S).	PAR VALUE	NUMBER OF SHARES, UNITS OR INTERESTS

PLEDGED DEBT INSTRUMENTS

COMMERCIAL TORT CLAIMS

ACKNOWLEDGED AND AGREED
as of the date first above written:

BIOPHARMA CREDIT PLC,
as Collateral Agent

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By _____
Name: Pedro Gonzalez de Cosio
Title: Managing Member

ANNEX 2
TO
GUARANTY AND SECURITY AGREEMENT

FORM OF JOINDER AGREEMENT

This JOINDER AGREEMENT, dated as of_____, 20____, is delivered pursuant to Section 8.6 of the Guaranty and Security Agreement, dated as of [_____], 2019, by and among GLOBAL BLOOD THERAPEUTICS, INC. ("Borrower"), [_____], as a Grantor, and the other Persons from time to time party thereto as Grantors, in favor of BIOPHARMA CREDIT PLC (together with its successors and permitted assigns, the "Collateral Agent") on behalf of Lenders and each of the other Secured Parties, (as such agreement may be amended, restated, supplemented or otherwise modified from time to time, the "Guaranty and Security Agreement"). Capitalized terms used herein without definition are used as defined in the Guaranty and Security Agreement.

By executing and delivering this Joinder Agreement, the undersigned, as provided in Section 8.6 of the Guaranty and Security Agreement, (a) hereby becomes a party to the Guaranty and Security Agreement as a "Grantor" and "Guarantor" thereunder with the same force and effect as if originally named as a Grantor and Guarantor therein and, without limiting the generality of the foregoing, hereby assumes all obligations and liabilities of a Grantor and a Guarantor thereunder and (b) as collateral security for the prompt and complete payment and performance when due (whether at stated maturity, by acceleration or otherwise) of the Secured Obligations of the undersigned, hereby pledges and hypothecates to the Collateral Agent for the benefit of Lenders and the other Secured Parties, and grants to the Collateral Agent for the benefit of Lenders and the other Secured Parties, a lien on and security interest in, all of its right, title and interest in, to and under the Collateral of the undersigned. The undersigned hereby agrees to be bound as a Grantor and a Guarantor for the purposes of the Guaranty and Security Agreement.

In connection with this Joinder Agreement, the undersigned has delivered to the Collateral Agent a completed Perfection Certificate duly executed by the undersigned. The information set forth in Annex 1-A[1] is hereby added to the information set forth in Schedules 1, 2 and 4 to the Security Disclosure Letter. By acknowledging and agreeing to this Joinder Agreement, the undersigned hereby agrees that this Joinder Agreement may be attached to the Guaranty and Security Agreement, the Perfection Certificate delivered herewith by the undersigned shall constitute a "Perfection Certificate" referred to in Section 4.6 of the Loan Agreement and that the Pledged Collateral listed on Annex 1-A to this Joinder Agreement shall be and become part of the Collateral referred to in the Guaranty and Security Agreement and shall secure all Secured Obligations of the undersigned.

The undersigned hereby represents and warrants that each of the representations and warranties contained in Article IV of the Guaranty and Security Agreement applicable to it is true and correct on and as the date hereof as if made on and as of such date.

1 Use same Annex 1-A as is attached in Annex 1 to the Guaranty and Security Agreement.

In witness whereof, the undersigned has caused this Joinder Agreement to be duly executed and delivered as of the date first above written.

[Additional Grantor]

By: _____
Name:
Title:

ACKNOWLEDGED AND AGREED
as of the date first above written:

BIOPHARMA CREDIT PLC,
as Collateral Agent

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By_____

Name: Pedro Gonzalez de Cosio
Title: Managing Member

ANNEX 3
TO
GUARANTY AND SECURITY AGREEMENT

FORM OF INTELLECTUAL PROPERTY SECURITY AGREEMENT

THIS [COPYRIGHT] [PATENT] [TRADEMARK] SECURITY AGREEMENT, dated as of _____, 20__, is made by _____ ("Grantor"), in favor of BIOPHARMA CREDIT PLC (together with its successors and permitted assigns, the "Collateral Agent") on behalf of Lenders and the other Secured Parties (as defined in the Loan Agreement referred to below).

W I T N E S S E T H:

WHEREAS, pursuant to the Loan Agreement, dated as of [_____], 2019 (as the same may be amended, restated, supplemented or otherwise modified from time to time, the "Loan Agreement"), by and among GLOBAL BLOOD THERAPEUTICS, INC. ("Borrower"), [_____] (as am additional Credit Party), BIOPHARMA CREDIT PLC (as the "Collateral Agent" and a "Lender"), and BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP (as a "Lender"), each Lender has agreed to make extensions of credit to Borrower upon the terms and subject to the conditions set forth therein;

WHEREAS, Grantor [(other than Borrower)] has agreed, pursuant to a Guaranty and Security Agreement dated as of [_____], 2019 in favor of the Collateral Agent for the benefit of Lenders and the other Secured Parties (as such agreement may be amended, restated, supplemented or otherwise modified from time to time, the "Guaranty and Security Agreement"), to guarantee the Obligations (as defined in the Loan Agreement) of Borrower; and

WHEREAS, Grantor is party to the Guaranty and Security Agreement pursuant to which Grantor is required to execute and deliver this [Copyright] [Patent] [Trademark] Security Agreement;

NOW, THEREFORE, in consideration of the mutual covenants, terms and conditions set forth herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree, intending to be legally bound, as follows:

Section 1. Defined Terms. Capitalized terms used herein without definition are used as defined in the Guaranty and Security Agreement.

Section 2. Grant of Security Interest in [Copyright] [Trademark] [Patent] Collateral. Grantor, as collateral security for the prompt and complete payment and performance when due (whether at stated maturity, by acceleration or otherwise) of the Secured Obligations, hereby mortgages, pledges and hypothecates to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, and grants to the Collateral Agent, for the benefit of Lenders and the other Secured Parties, a Lien on and security interest in, all of its right, title and interest in, to and under the following Collateral of Grantor, in each case, solely to the extent constituting Collateral (and excluding any Excluded Property) (the "[Copyright] [Patent] [Trademark] Collateral"):

(a) [all of its Copyrights and all IP Licenses and IP Ancillary Rights providing for the grant by or to Grantor of any right under any Copyright, including, without limitation, those referred to on Schedule 1 hereto;

(b) all renewals, reversions and extensions of the foregoing; and

(c) all income, royalties, proceeds and liabilities at any time due or payable or asserted under and with respect to any of the foregoing, including, without limitation, all rights to sue and recover at law or in equity for any past, present and future infringement, misappropriation, dilution, violation or other impairment thereof.]

or

(d) [all of its Patents and all IP Licenses and IP Ancillary Rights providing for the grant by or to Grantor of any right under any Patent, including, without limitation, those referred to on Schedule 1 hereto;

(e) all reissues, reexaminations, continuations, continuations-in-part, divisionals, renewals and extensions of the foregoing; and

(f) all income, royalties, proceeds and liabilities at any time due or payable or asserted under and with respect to any of the foregoing, including, without limitation, all rights to sue and recover at law or in equity for any past, present and future infringement, misappropriation, dilution, violation or other impairment thereof.]

or

(g) [all of its Trademarks and all IP Licenses and IP Ancillary Rights providing for the grant by or to Grantor of any right under any Trademark, including, without limitation, those referred to on Schedule 1 hereto, but excluding any “intent to use” Trademark applications for which a statement of use has not been filed (but only excluding such applications until such statement is filed);

(h) all renewals and extensions of the foregoing;

(i) all goodwill of the business connected with the use of, and symbolized by, each such Trademark; and

(j) all income, royalties, proceeds and liabilities at any time due or payable or asserted under and with respect to any of the foregoing, including, without limitation, all rights to sue and recover at law or in equity for any past, present and future infringement, misappropriation, dilution, violation or other impairment thereof.]

Section 3. Guaranty and Security Agreement. The security interest granted pursuant to this [Copyright] [Patent] [Trademark] Security Agreement is granted in conjunction

with the security interest granted to the Collateral Agent for the benefit of Lenders and the other Secured Parties, pursuant to the Guaranty and Security Agreement and Grantor hereby acknowledges and agrees that the obligations, rights and remedies of Grantor and of the Collateral Agent on behalf of Lenders and the other Secured Parties with respect to the security interest in the [Copyright] [Patent] [Trademark] Collateral made and granted hereby are more fully set forth in the Guaranty and Security Agreement, the terms and provisions of which are incorporated by reference herein as if fully set forth herein.

Section 4. Grantor Remains Liable. Grantor hereby agrees that, anything herein to the contrary notwithstanding, Grantor shall assume full and complete responsibility for the prosecution, defense, enforcement or any other reasonably necessary actions in connection with their [Copyrights] [Patents] [Trademarks] and IP Licenses subject to a security interest hereunder.

Section 5. Counterparts. This [Copyright] [Patent] [Trademark] Security Agreement may be executed in any number of counterparts and by different parties in separate counterparts, each of which when so executed shall be deemed to be an original and all of which taken together shall constitute one and the same agreement. Signature pages may be detached from multiple separate counterparts and attached to a single counterpart.

Section 6. Governing Law. This [Copyright] [Patent] [Trademark] Security Agreement and the rights and obligations of the parties hereto shall be governed by, and construed and interpreted in accordance with, the law of the State of New York without regard to any principle of conflicts of law that could require the application of the law of any other jurisdiction.

IN WITNESS WHEREOF, Grantor has caused this [Copyright] [Patent] [Trademark] Security Agreement to be executed and delivered by its duly authorized officer as of the date first set forth above.

Very truly yours,
[GRANTOR] as Grantor

By: _____
Name:
Title:

ACCEPTED AND AGREED
as of the date first above written:

BIOPHARMA CREDIT PLC,
as Collateral Agent

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By _____
Name: Pedro Gonzalez de Cosio
Title: Managing Member

SCHEDULE I
TO
[COPYRIGHT] [PATENT] [TRADEMARK] SECURITY AGREEMENT

[Copyright] [Patent] [Trademark] Registrations

1. REGISTERED [COPYRIGHTS] [PATENTS] [TRADEMARKS]

[Include Registration Number and Date]

2. [COPYRIGHT] [PATENT] [TRADEMARK] APPLICATIONS

[Include Application Number and Date]

3. [IP LICENSES

[Include complete legal description of agreement (name of agreement, parties and date)]]

ANNEX 4
TO
GUARANTY AND SECURITY AGREEMENT
FORM OF UNCERTIFICATED STOCK CONTROL AGREEMENT

This UNCERTIFICATED STOCK CONTROL AGREEMENT (this "**Agreement**"), dated as of_____, 20____, is made by and among [APPLICABLE GRANTOR], a [JURISDICTION OF ORGANIZATION] [ENTITY TYPE] (the "**Grantor**"), BIOPHARMA CREDIT PLC, a public limited company organized under the laws of England and Wales, as collateral agent on behalf of the Secured Parties (the "**Collateral Agent**"), and [APPLICABLE INTEREST ISSUING COMPANY], a [JURISDICTION OF ORGANIZATION] [ENTITY TYPE] (the "**Issuer**"). All capitalized terms used but not otherwise defined herein shall have the meanings assigned to such terms in the Security Agreement (as defined below) or the Loan Agreement (as defined below), as applicable.

WHEREAS, GLOBAL BLOOD THERAPEUTICS, INC., a Delaware corporation (as "**Borrower**"), [_____] (as an additional Credit Party), the Collateral Agent and the Lenders have entered into that certain Loan Agreement, dated as of [_____], 2019 (as may be amended, restated, supplemented or otherwise modified from time to time, the "**Loan Agreement**");

WHEREAS, the Grantor is the registered holder of [DESCRIBE PLEDGED UNCERTIFICATED STOCK] issued by the Issuer (the "**Pledged Stock**");

WHEREAS, pursuant to the Guaranty and Security Agreement, dated as of [_____], 2019, by and among the Grantor, the Collateral Agent and the other parties thereto (as amended, amended and restated, supplemented or otherwise modified from time to time, the "**Security Agreement**"), the Grantor has granted a continuing Lien on and security interest (the "**Security Interest**") in, all of its right, title and interest in, to and under the Pledged Stock (other than Excluded Equity Interests), whether now existing or hereafter arising or acquired; and

WHEREAS, it is a condition precedent to the making and maintaining of the Term Loans by Lenders under the Loan Agreement that the parties hereto execute and deliver this Agreement in order to perfect a first priority Security Interest in the Pledged Stock.

NOW, THEREFORE, in consideration of the mutual covenants, terms and conditions set forth herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree, intending to be legally bound, as follows:

1. The Issuer confirms that:

(a) The Pledged Stock is Equity Interests that are not represented by certificates;

(b) The Issuer is the issuer of the Pledged Stock and the Grantor is registered on the books and records of the Issuer as the registered holder of the Pledged Stock; and

(c) The Security Interest in the Pledged Stock is registered on the books and records of the Issuer.

2. The Grantor hereby irrevocably agrees that, for so long as this Agreement remains in effect, the Collateral Agent, for the benefit of Lenders and the other Secured Parties, shall have exclusive control of the Pledged Stock. In furtherance of such agreement, the Grantor hereby irrevocably authorizes and directs the Issuer, and the Issuer hereby agrees:

(a) Subject to the provisions of Section 3 hereof, to comply with any and all written instructions delivered to the Issuer which directs that the transfer of any or all of the Pledged Stock to the Collateral Agent be registered on the books and records of the Issuer in the name of the Collateral Agent as the holder thereof, for the benefit of Lenders and the other Secured Parties, without further consent by the Grantor or any other Person; and

(b) Subject to the provisions of Section 3 hereof, not to comply with any instructions relating to any or all of the Pledged Stock originated by any Person other than the Collateral Agent, on behalf of Lenders and the other Secured Parties, or a court of competent jurisdiction. In the event of any conflict between any instruction originated by the Collateral Agent and any instruction originated by any other Person, the Issuer shall comply only with the instruction originated by the Collateral Agent.

3. In addition to, and not in lieu of, the obligation of the Issuer to honor instructions as agreed in Section 2 hereof, the Issuer and the Collateral Agent hereby agree as follows:

(c) Subject to the rights of the Grantor described herein, the Issuer agrees that, from and after the date hereof, the Pledged Stock shall be under the exclusive dominion and control of the Collateral Agent;

(d) So long as the Issuer has not received a written notice from the Collateral Agent that it is exercising exclusive control over the Pledged Stock (a "**Notice of Exclusive Control**"), the Issuer may comply with instructions of the Grantor concerning the Pledged Stock, which Notice of Exclusive Control shall only be given by the Collateral Agent following the occurrence and during the continuance of an Event of Default. After the Issuer receives a Notice of Exclusive Control from the Collateral Agent, the Issuer will not accept any instructions concerning the Pledged Stock from any Person other than the Collateral Agent, unless otherwise ordered by a court of competent jurisdiction; and

(e) Until the Issuer receives a Notice of Exclusive Control, the Grantor shall be entitled to direct the Issuer with respect to voting the Pledged Stock.

4. This Agreement shall not subject the Issuer to any obligation or liability except as expressly set forth herein and under any Requirements of Law. In particular, the Issuer need not investigate whether the Collateral Agent is entitled under the Security Agreement or otherwise to give an instruction or Notice of Exclusive Control.

5. The Issuer hereby represents, warrants and covenants with the Collateral Agent that:

(f) This Agreement has been duly authorized, executed and delivered by the Issuer and constitutes a legal, valid and binding obligation of the Issuer enforceable in accordance with its terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium or other similar laws affecting creditors' rights generally and subject to equitable principles (regardless of whether enforcement is sought in equity or at law);

(g) The Issuer has not entered into, and until termination of this Agreement will not enter into, any agreement with any other Person relating to the Pledged Stock pursuant to which it has agreed, or will agree, to comply with instructions provided by such Person. The Issuer has not entered into any other agreement with the Grantor purporting to limit or condition the obligation of the Issuer to comply with instructions as agreed in Section 3 hereof;

(h) Except for the claims and interests of the Collateral Agent, on behalf of Lenders and the other Secured Parties, and the Grantor in the Pledged Stock, the Issuer does not know of any claim to, or interest in, the Pledged Stock (except to the extent constituting Permitted Liens). If any Person asserts any Lien or adverse claim (including any writ, garnishment, judgment, attachment, execution or similar process) against the Pledged Stock (other than Permitted Liens), the Issuer will promptly notify the Collateral Agent and the Grantor thereof;

(i) There is no agreement (except this Agreement) between the Issuer and the Grantor or among the Issuer, the Grantor and any third Person with respect to the Pledged Stock [except for [IDENTIFY RELEVANT AGREEMENTS] (the "**Existing Agreements**")]. In the event of any conflict between this Agreement (or any portion hereof) and any other such agreement [(including any Existing Agreement)] with respect to the Pledged Stock, whether now existing or hereafter entered into, the terms of this Agreement shall prevail; and

(j) The granting by the Grantor of the Security Interest in the Pledged Stock to the Collateral Agent for the benefit of Lenders and the other Secured Parties does not violate the Operating Documents or any other agreement governing the Issuer or the Pledged Stock.

6. This Agreement shall be binding upon, and shall inure to the benefit of, the parties hereto and their respective successors and assigns.

7. Each notice, request or other communication to a party hereto under this Agreement shall be in writing, will be sent to such party's address set forth under its name below or to such other address as such party may notify the other parties hereto and will be effective on receipt.

8. No amendment or modification of this Agreement or waiver of any right hereunder shall be binding on any party hereto unless it is in writing and is signed by all the parties hereto.

9. The rights and powers granted herein to the Collateral Agent (a) have been granted in order to perfect the Security Interest in the Pledged Stock, (b) are powers coupled with an interest and (c) will not be affected by any bankruptcy of the Grantor or any lapse in time. The obligations of the Issuer hereunder shall continue in effect until the Collateral Agent has notified the Issuer in writing that the Security Interest in the Pledged Stock has been terminated pursuant to the Security Agreement.

10. This Agreement shall be governed by and construed in accordance with the laws of the [ISSUER'S JURISDICTION OF ORGANIZATION].

11. If any term or provision of this Agreement is invalid, illegal or unenforceable in any jurisdiction, such invalidity, illegality or unenforceability shall not affect any other term or provision of this Agreement or invalidate or render unenforceable such term or provision in any other jurisdiction.

12. This Agreement may be executed in counterparts.

[Signature Page Follows]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

[GRANTOR]
By:_____
Name:_____
Title:_____

Address for Notices:

[ISSUER]
By:_____
Name:_____
Title:_____

Address for Notices:

BIOPHARMA CREDIT PLC,
a public limited company

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By _____
Name: Pedro Gonzalez de Cosio
Title: Managing Member

Address for Notices:

BIOPHARMA CREDIT PLC
c/o Beaufort House
51 New North Road
Exeter EX4 4EP
United Kingdom
Attention: Company Secretary
Telephone: +44 01 392 477 500
Facsimile: +44 01 392 253 282

with copies (which shall not constitute notice) to:

Pharmakon Advisors LP
110 East 59th Street, #3300
New York, NY 10022
Attn: Pedro Gonzalez de Cosio
Phone: +1 (212) 883-2296
Fax: +1 (917) 210-4048
Email: pg@PharmakonAdvisors.com

and

Akin Gump Strauss Hauer & Feld LLP
One Bryant Park
New York, NY 10036-6745
Attn: Geoffrey E. Secol; Jonathan Pavlich
Phone: (212) 872-8081; (212) 872-8013
Fax: (212) 872-1002
Email: gsecol@akingump.com; jpavlich@akingump.com

EXHIBIT D

COMMITMENTS; NOTICE ADDRESSES

[***]

EXHIBIT E

COMPLIANCE CERTIFICATE

TO: BIOPHARMA CREDIT PLC

FROM: GLOBAL BLOOD THERAPEUTICS, INC.

The undersigned authorized officer of GLOBAL BLOOD THERAPEUTICS, INC., a Delaware corporation ("**Borrower**") hereby certifies, solely in his/her capacity as a Responsible Officer of Borrower and not in his/her personal capacity, that in accordance with the terms and conditions of the Loan Agreement (the "**Loan Agreement**"; capitalized terms used, but not defined herein having the meanings given them in the Loan Agreement) dated as of [_____] by and among Borrower, the Guarantor Subsidiaries from time to time party thereto, BIOPHARMA CREDIT PLC, a public limited company incorporated under the laws of England and Wales (as "**Collateral Agent**") and the Lenders:

(i) The Credit Parties are in complete compliance for the period ending _____ with all required covenants except as noted below;

(ii) No Default or Event of Default has occurred and is continuing, except as noted below;

(iii) Each Credit Party and each of its Subsidiaries has timely filed all U.S. federal income Tax returns and other material Tax returns and reports (or extensions thereof) of each Credit Party and each of its Subsidiaries required to be filed by any of them and such returns and reports are correct in all material respects, and has timely paid all material Taxes owed which are due and payable by such Credit Party or Subsidiary or upon their respective properties, assets, income, businesses and franchises, except as otherwise permitted pursuant to the terms of Section 4.10 or Section 5.3 of the Loan Agreement;

(iv) No Liens have been levied or claims made against any Credit Party or any of its Subsidiaries relating to unpaid employee payroll or benefits of which (a) such Credit Party has not previously provided written notification to the Collateral Agent or (b) which do not constitute Permitted Liens; and

Attached are the required documents, if any, supporting our certification(s). The undersigned Responsible Officer on behalf of Borrower further certifies that the attached financial statements fairly present, in all material respects, the consolidated financial condition, results of operations and cash flows of Borrower and its Subsidiaries as of applicable the dates and for the applicable periods in accordance with Applicable Accounting Standards consistently applied (taking into account the provisions of Section 1 of the Loan Agreement if and to the extent applicable).

Date: _____

[Signature page follows]

GLOBAL BLOOD THERAPEUTICS, INC.,
as Borrower

By _____
Name: _____
Title: _____

Exhibit 21.1

SUBSIDIARIES OF REGISTRANT

Not applicable.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Global Blood Therapeutics, Inc.:

We consent to the incorporation by reference in the registration statements (Nos. 333-206329, 333-210475, 333-215732, 333-222803, 333-226051, 333-229392, 333-232427 and 333-236042) on Form S-8, the registration statement (No. 333-214088) on Form S-3, and the registration statement (No. 333-220127) on Form S-3 ASR of Global Blood Therapeutics, Inc. and subsidiary of our report dated February 26, 2020, with respect to the consolidated balance sheets of Global Blood Therapeutics, Inc. and subsidiary as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2019, and the related notes, and the effectiveness of internal control over financial reporting as of December 31, 2019, which report appears in the December 31, 2019 annual report on Form 10-K of Global Blood Therapeutics, Inc. and subsidiary.

Our report refers to a change in the method of accounting for leases as of January 1, 2019 due to the adoption of FASB Accounting Standards Update 2016-02, *Leases (Topic 842)*.

/s/ KPMG LLP

San Francisco, California
February 26, 2020

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ted W. Love, certify that:

1. I have reviewed this Annual Report on Form 10-K of Global Blood Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant 's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant 's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant 's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2020

By: /s/ Ted W. Love

Ted W. Love, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jeffrey Farrow, certify that:

1. I have reviewed this Annual Report on Form 10-K of Global Blood Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2020

By: /s/ Jeffrey Farrow
Jeffrey Farrow
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Global Blood Therapeutics, Inc. (the "Company") on Form 10-K for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Ted W. Love, President and Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 26, 2020

By: /s/ Ted W. Love
Ted W. Love, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Global Blood Therapeutics, Inc. (the "Company") on Form 10-K for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Jeffrey Farrow, Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 26, 2020

By: /s/ Jeffrey Farrow
Jeffrey Farrow
Chief Financial Officer
(Principal Financial Officer)